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TITLE: Human Leukocyte Antigen (HLA) Genotype as a Contributor to Racial/Ethnic Differences in Breast Cancer: A Population-Based Molecular Epidemiologic Study

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14. ABSTRACT

As both breast cancer incidence and the highly polymorphic genes for the human leukocyte antigen (HLA) component of the immune system differ across racial/ethnic groups, HLA may be a biologically based risk factor for breast cancer and explain some of its racial/ethnic variation. In a population-based series of 915 post-menopausal white, black and Hispanic breast cancer cases and controls, we determined HLA class I (A, B) and class II (DR, DQ) genotypes through DNA methodology and calculated age- and risk-factor-adjusted odds ratios to estimate allele-specific risks. We found moderate associations of HLA alleles with breast cancer overall but varying with race/ethnicity. Overall, breast cancer risk was suggestively increased for allele A-33, suggestively decreased for alleles B-13 and B-39, and doubled for the DR-DQ haplotype 0803. In whites, A-23 increased risk. In blacks, A-32, A-33 and DQB-5 increased risk, while DRB-9 reduced risk. In Hispanics, B-40 increased risk, while A-01, B-07, and B-45 decreased risk. Some associations were modified by disease stage at diagnosis, ER status of tumors, and breast cancer family history. Associations noted for A-01, A-23, A-32, B-07, DRB1-01, DQB1-02 and DQB1-05 were consistent with observed racial/ethnic incidence differentials, but other associations were in contradictory directions. Our findings, limited by sample size and multiple comparisons, support a possible but complex role of HLA or linked loci in breast cancer occurrence and perhaps the racial/ethnic variation in its incidence.

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Human leukocyte antigen (HLA), genetic epidemiology, molecular epidemiology, Race/ethnicity, breast cancer, immunosurveillance

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INTRODUCTION:

The incidence and mortality burdens of breast cancer differ markedly across racial/ethnic groups, particularly in post-menopausal women, but known risk factors do not explain all of this variation, or the majority of breast cancers. The human leukocyte antigen (HLA) component of the immune system, encoded by highly polymorphic genes that vary substantially across racial/ethnic groups and have been related to numerous diseases, has not been much examined for non-viral cancers, including breast cancer. Therefore, to examine for breast cancer whether genetically determined aspects of immune function represent biologically based risk factors and explain a portion of its variation by race/ethnicity, we took advantage of already collected DNA and epidemiologic data for a population-based series of post-menopausal white, black and Hispanic incident invasive breast cancer cases and community controls from Northern California. With the DNA, we used PCR-based, immobilized probe (sequence-specific oligonucleotide) typing to assign HLA genotypes to 915 cases and controls frequency-matched for age and race/ethnicity. We assessed whether HLA genotypes are associated with breast cancer overall and in three racial/ethnic groups by comparing allele or haplotype distributions between cases and controls and quantifying the extent of association with odds ratios adjusted for potential confounders. We also determined if associations differed among the racial/ethnic groups by comparing allele-specific relative frequency distributions, adjusted odds ratios, and population prevalences of risk-associated alleles. In addition, using these same approaches, we explored whether HLA associations related to tumor characteristics, namely stage at diagnosis and estrogen-receptor (ER) status.

BODY:

Task 1: Develop study subject database from existing databases

a. *Apply eligibility criteria to the Bay Area Breast Cancer Study (BABCS) study database to select post-menopausal, blood-providing study subjects and extract relevant epidemiologic and specimen-tracking data.*

We identified 426 cases and 489 controls who had self-described as post-menopausal in a previous in-person interview[1], and for whom DNA was available.

b. *Link study patients to Greater Bay Area Cancer Registry database to obtain demographic, clinical and tumor characteristics.*

We conducted the linkage and produced a study database. The study subjects and their characteristics are presented in Table 1. There were few differences between cases and controls for any risk factors; only age at menarche for Hispanics and parity for blacks were associated with breast cancer. ER status was unknown for tumors of 13.8% of white women, 20.1% of black women, and 14.3% of Hispanic women. As none of the study variables was a significant predictor of unknown ER status, we excluded these cases from analyses stratified by ER status.

c. *Install linked study subject database into study tracking database, creating study identification (ID) numbers.*

We produced a study tracking database with IRB-approved study ID's.

Task 2: Obtain DNA samples from storage at USC

a. *Transmit electronic file of study-subject BABCS tracking ID numbers to Dr. Engles' lab at USC.*

We submitted BABCS tracking numbers to USC.

b. *Request DNA for each patient be transmitted in 96-well trays to Dr. Erlich's lab, labeled only by unique specimen ID number.*

DNA samples, each comprising 1 microgram of DNA that had been dried down, were transmitted from Dr. Ingles' lab to Dr. Erlich's staff in 11 plates.

c. Track DNA specimen transmission.

Transmission of the DNA was tracked and its receipt was acknowledged by Dr. Erlich's staff.

Task 3: HLA-type DNA specimens

a. Amplify class I (A,B) and class II (DQ,DR) loci.

Class I (A,B) and class II (DR, DQ) loci were amplified.

b. Type using immobilize probe linear arrays.

This task was completed.

c. Scan probe reactivity patterns and convert patterns to genotype.

This task was completed.

d. Record assay results on Excel spreadsheet and transmit back to NCCC.

A spreadsheet with all genotyping results was transmitted to NCCC; DR-DQ haplotypes were specified.

Task 4: Create study database (months 19)

a. Merge study database, including interview and registry data, with HLA typing data.

A database including interview data, cancer registry data and HLA typing data was produced.

b. Link study database to Greater Bay Area Cancer Registry database to obtain most current patient vital status.

We obtained updated vital status for patients as of 2004. However, because of the pre-selection of subjects on vital status for the original case-control study from which study data and DNA came, and the relatively high survival rate for breast cancer, only 11.0% of the cases were deceased. Given this small sample size together with the very small numbers of patients in most allele-specific groups, a survival analysis would not have been informative.

c. Strip database of all subject identifiers.

The analytic database was stripped of identifiers.

Task 5: Statistical analysis (months 20-23)

a. Compare allele frequencies for HLA-A, -B, -DQ and -DR separately for each race.

We first conducted allele-specific analyses at the genotype (i.e., 2N) and phenotype (individual) levels. To determine allele carrier or non-carrier status at the phenotype level, we considered any person who was homozygotic or heterozygotic for a specific allele to be a carrier of that allele, and persons without a copy of the allele to be non-carriers. Then, we compared relative frequency distributions of alleles for cases and controls testing for significant differences (i.e., $p<=0.05$) with X^2 statistics or Fisher's exact test, as needed. Because many such tests were involved, we also made Bonferroni-type corrections for multiple comparisons for each table, but we present the uncorrected probabilities because of the conservative nature of this correction and the fact that this is the first in-depth population-based examination of HLA genotype and breast cancer risk and therefore serves in part as an exploratory exercise. Finally, we identified alleles and DR-DQ haplotypes of interest for their possible association with breast cancer by calculating Z-scores for case-control differences in allele prevalences and then selecting the five alleles with Z-scores corresponding to the largest differences for each locus. Because the number of alleles significantly associated with breast cancer was small, the choice to pursue five with the greatest differences was conservative; in a few circumstances, we selected more than five alleles for more in-depth analysis.

a. Compute odds ratios and 95% confidence intervals

We estimated breast cancer risk at the phenotypic (individual) level associated with each of the five (or more) selected alleles and haplotypes using logistic regression to calculate odds ratios and 95% confidence intervals adjusted for age at diagnosis, race/ethnicity, and other variables, as described below.

c. Compare across racial/ethnic groups HLA associations significant in any racial/ethnic group.

This task was completed using relative frequency distributions and statistical tests as described in 5a above for analyses stratified by racial/ethnic group (white, black, Hispanic) and in 5e below.

d. Examine whether relationships are confounded by other epidemiologic or tumor features.

Examinations of confounding by risk factors were undertaken at the phenotype level by stratifying allele relative frequencies for controls by suspected risk factors (age at menarche (less than 12 years, 12 years or older), age at 1st full-term pregnancy (over age 30 or nulliparous (based on similar breast cancer risks), less than age 30), cumulative duration of lactation among parous women (less than 5 months, equal to or greater than 5 months)), and self-reported family history of breast cancer (yes, no). Because family history of breast cancer may reflect the impact of genetic predisposition, we also stratified our data by this classification. To determine whether HLA associations differed by tumor characteristics (stage of disease at diagnosis, ER status), we conducted analyses within the strata of these features (i.e., localized stage and regional/remote stage; ER-positive and ER-negative) based on comparing stratum-specific cases to all controls; tables present only those allele frequencies for which case-control differences were significant at p<=0.05. Comparisons of findings across family history and tumor characteristics strata were conducted descriptively. Because of the small cell sizes, we did not undertake stratified analyses for DR-DQ haplotypes.

e. Conduct logistic regression to predict breast cancer risk associated with the alleles of interest with control for confounders

First, we estimated breast cancer risks for all alleles and DR-DQ haplotypes with the five (or more) highest Z-scores in each of the racial/ethnic groups for all women together using logistic regression to calculate odds ratios and 95% confidence intervals adjusted for age at diagnosis, race/ethnicity, the reproductive factors listed above, and self-reported family history of breast cancer. Then, to explore whether these associations differed across racial/ethnic groups, we computed allele-specific odds ratios for breast cancer in each racial/ethnic group, adjusted for age at diagnosis, the reproductive factors, and self-reported family history of breast cancer. We examined whether the magnitude or direction of the OR for a significant allele varied across the three racial/ethnic groups, indicating a difference in effect, or alternatively, if there were differences in the population prevalences across alleles irrespective of whether the ORs were similar across racial/ethnic groups, indicating a potential impact on risk from variation in population prevalences. Finally, we tested formally for race-allele interactions in the fully adjusted models to establish whether pairs of race-specific ORs were significantly different.

Task 6: Summarize study findings for presentation and submission for publication in literature (months 23-24)

Preliminary study findings were presented in two posters and one oral presentation at scientific meetings, as listed below in “Reportable Outcomes”. A manuscript summarizing study findings is in preparation.

Study Findings

Study findings are presented below by HLA class for all women together and then by racial/ethnic group. Case-control differences in allele or haplotype prevalences were observed and were noted to vary by race/ethnicity and tumor characteristics, but no associations remained statistically significant after adjustment for multiple comparisons.

Class I A:

All women: For all post-menopausal women (i.e., combined across racial/ethnic groups), HLA class I A alleles were associated with breast cancer only for A-23 (table 2). In logistic regression models (table 3), the odds ratio for A-23 adjusted for age, race/ethnicity, and all risk factors (including family history) was elevated but not significantly, and A-33 was marginally associated with an increased risk of breast cancer.

Women by race/ethnicity: Associations differed by race/ethnicity (table 4). A-23 was associated with breast cancer only in whites, while A-32 was significantly associated with breast cancer only in black women; this case-control difference was close to being statistically significant even after correction for multiple comparisons (p=0.003 required). Logistic regression (table 5) showed an elevated breast cancer risk with A-23 for white women and for A-32 in black women. Tests for interaction showed that the risk for A-32 was significantly different in black women than white women (p=0.02) or Hispanic women (p=0.01). Hispanic women with A-01 had a significantly decreased breast cancer risk, which was marginally different than the risk in whites (p=0.06).

Class I B:

All women: For all study subjects combined, alleles prevalences were significantly lower in cases than controls among carriers B-13, B-39 and B-50 (table 6). Logistic regression (table 7) revealed a significantly reduced risk of breast cancer in women positive for B-13 and for B-39.

Women by race/ethnicity: Associations differed across racial/ethnic groups (table 8). None of the three alleles associated with breast cancer overall (B-13, B-39, B-50) was significantly linked to breast cancer in any racial/ethnic group, although for B-39, the allele prevalence was suggested to be lower for cases than controls for whites and Hispanics but not for black women. Significant associations with breast cancer were noted for B-44 for black women and for B-07 for Hispanic women. However, logistic regression (table 9) showed statistically significant breast cancer risks only in Hispanic women; for those with B-07, breast cancer risk was reduced, and this risk was significantly different than the risk for white women (p=0.04) or black women (p=0.02). Risk also was decreased for Hispanic women with B-45 and increased for those with B-40, although confidence intervals for both estimates included one.

Class II DRB1:

All women: There were no significant or suggestive allele-specific associations with breast cancer of class II DRB1 alleles at the level of prevalences (table 10) or risk models (table 11).

Women by race/ethnicity: Breast cancer was associated in black women with DRB1-09 in allele frequencies (table 12) and logistic regression (table 13), with no similar protective effect noted for whites or Hispanics. The OR in blacks was significantly different than that in both other groups (p=0.02, p=0.02).

Class II DQB1:

All women: There were no allele-specific associations of class II DQB1 alleles (table 14); findings were similarly negative with logistic regression controlling for age, race/ethnicity and risk factors (table 15).

Women by race/ethnicity: Among racial/ethnic groups (table 16), there was a suggestive association with breast cancer for Hispanics with DQB1-02, but it was not significant in logistic regression (table 17). In black women, breast cancer risk was suggested to be increased for those with DQB1-05, and the risk estimate for this allele was significantly different (p=0.04) from that in Hispanic women.

Class II DR-DQ haplotypes:

All women: For breast cancer overall, the only class II DR-DQ haplotype association with breast cancer occurred for DRDQ-0803, as noted in frequency distributions (table 18) and logistic regression models (table 19). For many haplotypes, sample sizes were too small to permit stable risk models.

By race/ethnicity: Across racial/ethnic groups (table 20), there was a suggestive association with breast cancer in black carriers of DRDQ-0902; this haplotype did not occur in white women and did not show a similar association pattern in Hispanics. Logistic regression (table 21) confirmed a significant protective effect of 0902 in black women. DRDQ-0803 was suggested to double breast cancer risk in all groups, although at a level approaching statistical significance only among blacks.

By tumor features:

Table 1 indicates that the majority of cases was diagnosed with localized disease; similarly, among cases with known ER status, the majority was ER-positive, although less so for black women (65.1%) than for white (89.3%) or Hispanic women (80.7%). In addition, stage and ER status were related, with localized stage more likely than later stage to involve ER-positive disease in whites and blacks: The proportions of localized and regional/remote disease cases, respectively, that had ER-positive tumors were 92.2% and 79.3% in whites (p=0.05), 71.4% and 48.3% in blacks (p=0.03) and 79.5% and 83.3% in Hispanics (p=0.63).

Class I A by stage: When cases of all races combined were stratified by their disease stage at diagnosis and compared to all controls (table 22), associations with A-23 and A-33 were limited to women with localized disease. In women with later-stage disease, allele prevalences were significantly lower for A-11 and significantly higher for A-33 in cases than in all controls. In logistic regression, risk of localized disease was found to be elevated for A-23 and A-33 and marginally reduced for A-01, while risk of advanced disease was marginally reduced for A-11 and marginally elevated for A-30 (table 23).

For whites, the effect of A-23 was apparent across stage (table 24). However, in blacks (table 25), A-32 and A-33 were associated with localized but not advanced breast cancer. In Hispanics (table 26), the association with A-01 also was limited to localized disease. In logistic regression (tables 27, 28), the OR for A-23 was significantly elevated for whites, but in a similar direction for blacks and Hispanics. For A-32, increased breast cancer risk in blacks was apparent across stage although significantly only for localized disease. In black women, A-33 was associated with a significantly elevated risk of localized breast cancer. In Hispanic women, A-01 was associated with a markedly reduced risk of localized breast cancer.

Class I A by ER status: For ER-positive cases (table 29), the prevalence of A-11 was significantly lower in cases than in all controls. For ER-negative cases, this pattern occurred for A-1, while A-33 was more prevalent in cases than in all controls. In logistic regression (table 30), A-1 was associated with an approximate halving of risk of ER-positive disease, while A-33 nearly tripled risk of ER-negative disease.

In white women, the effects of A-11, A-23 and A-24 were limited to women with ER-positive tumors (table 31). For black women (table 32), the effect of A-32 was apparent irrespective of ER status of tumor, while A-33 was significantly associated only with ER-negative tumors. For Hispanics, there were no significant case-control distributions for either ER status (table 33). Logistic regression (tables 34, 35) showed that, for white women, A-11 and A-24 were both associated with a halving of risk for ER-positive disease. For black women, risk was elevated for A-32 for both ER-positive and ER-negative disease, and for A-33 for ER-negative disease, although with wide confidence intervals.

Class I B by stage: Associations with B-13, B-39 and B-50 were apparent for both localized and later-stage disease, albeit significantly only for the former (table 36). In logistic regression models for localized disease (table 37, left-hand columns), B-13 and B-15 were marginally associated with risk, while B-41 increased risk. For later-stage disease, B-44 was suggested to increase risk. In white women (table 38), B-58 was associated with regional/remote breast cancer. For black women (table 39), class I B associations did not vary significantly by disease stage. For Hispanic women (table 40), B-35 was associated with later-stage breast cancer, while B-40 appeared more strongly associated with localized than regional/remote disease. Logistic regression models (tables 41, 42) showed significant findings in Hispanics for B-35 for late-stage disease and B-40 for localized disease but with risks in similar directions for both disease stages.

Class I B by ER status: Compared to all controls, ER-positive but not ER-negative cases had significantly lower prevalences of B-42 (table 43), and ER-negative but not ER-positive cases had higher prevalences than

controls of B-15 and B-41. In logistic regression (table 44), only B-41 remained significantly associated with ER-negative disease. In white women (table 45), B-07 appeared to be associated only with ER-negative breast cancer. For black women (table 46), the effects of B-07 and B-42 occurred most markedly for ER-positive tumors. In Hispanic women (table 47), B-52 was associated only with ER-negative breast cancer. In logistic regression models (table 48), B-07 in black women was associated with a significantly increased risk of ER-positive breast cancer only, while the effect of B-42 was not statistically significant. Risks of ER-negative breast cancer were significantly increased in Hispanic women with B-41 and B-52, albeit with wide confidence intervals around the risk estimates (table 49).

Class II DRB1 by stage: There were no associations with DRB1 for all cases grouped by disease stage and compared to all controls overall (tables 50, 51) or among white women (table 52). For black women (table 53), DRB1-03 and DRB1-16 showed significant case-control prevalence differences only for localized disease. In Hispanics (table 54), DRB1-08 was associated only with localized-stage breast cancer. Logistic regression models (tables 55, 56) showed that DRB1-03 marginally reduced risk of localized breast cancer for black women, and DRB1-08 doubled the risk of localized-stage breast cancer in Hispanic women.

Class II DRB1 by ER status: There were no associations with DRB1 alleles for all cases grouped by tumor ER status (tables 57, 58) and compared to controls, or for white women (table 59). For black women (table 60), the effect of DRB1-01 was limited to ER-negative disease; the effect of DRB1-03 was stronger for ER-negative tumors but in a similar direction for ER-positive tumors; the effect of DRB1-09 was significant only for ER-positive disease, although a similar effect was present for ER-negative breast cancer; and the effect of DRB1-16 was limited to ER-positive tumors. In Hispanics (table 61), DRB1-08 was associated only with ER-positive tumors, and DRB1-09 only with ER-negative tumors. Logistic regression (tables 62, 63) confirmed a suggestively increased risk for ER-negative breast cancer for black carriers of DRB1-01 and a suggestively reduced risk for carriers of DRB1-03. For Hispanic women, DRB1-08 doubled the risk of ER-positive breast cancer, and DRB1-09 increased the risk of ER-negative disease, although confidence intervals were very wide for the latter estimate.

Class II DQB1 by stage: DQB1 alleles were not associated with localized or remote/regional-stage breast cancer overall (tables 64, 65) or in white women (table 66). In black women, DQB1-05 frequencies were higher for cases than all controls for localized disease only. In Hispanics, case-control prevalence differences occurred for DQB1-02, DQB1-04 and DQB1-05 for cases with localized but not regional/remote disease. These observations persisted in logistic regression (tables 67, 68).

Class II DQB1 by ER status: DQB1 alleles were not associated with ER-positive or ER-negative breast cancer overall (tables 69, 70) or in white women (table 71). For black women, DQB1-02 showed case-control prevalence differences only for ER-negative tumors, and DQB1-05 was associated with breast cancer more strongly for ER-negative tumors, although in a similar direction for ER-positive tumors. In Hispanics, DQB1-04 was associated only with ER-positive breast cancer, while DQB1-05 appeared to be more strongly associated for ER-negative tumors. Logistic regression models (table 72, 73) confirmed a reduced risk of ER-negative breast cancer in black women with DQB1-02; an elevated risk for ER-positive breast cancer for Hispanic women with DQB1-04; and an increased risk of ER-negative breast cancer in black women with DQB1-05 but decreased risk of ER-negative breast cancer for Hispanic women with DQB1-05.

By family history

Case-control differences in allele prevalences appeared to vary by self-reported family history of breast cancer, as described below, although the relatively low prevalence of a positive family history (see table 1) reduced statistical power for detecting associations in these stratified analyses.

Class I A: The association with A-23 overall was limited to women without a self-reported family history of breast cancer (10.7% vs 5.9%, p=0.02; 7.4% vs 11.5%, p=0.42, family history). In Hispanics, A-02 was directly associated in women without a family history of breast cancer (57.6% vs 47.2%, p=0.05) but indirectly associated in women with a positive history (30.0% vs 61.1%, p=0.05); A-11 was related to risk in women with a family history (0.0% vs 22.1%, p=0.04) but not in women with no family history (7.6% vs 7.8%, p=0.94).

Class I B: B-alleles that impacted risk for women of all races without a family history included B-27 (3.1% vs 6.6%, p=0.02, no family history; 10.3% vs 6.7%, p=0.47, family history); B-39 (5.1% vs 9.7%, p=0.02; 4.4% vs 0.0%, p=0.25); B-44 (22.5% vs 16.3%, p=0.03; 25.0% vs 35.0%, p=0.22); B-50 (1.4 vs 4.0, p=0.03; 2.9% vs 1.7%, p=0.63). For women of all races reporting a family history, breast cancer was associated with B-53 (9.6% vs 9.0%, p=0.78, no family history; 2.9% vs 15.0%, p=0.02, family history). In racial/ethnic groups, a negative breast cancer family history impacted the association with breast cancer of B-44 in blacks (22.6% vs 12.4%, p=0.04 for no family history; 22.2% vs 26.3%, p=0.77 for a family history) and of B-45 in Hispanics (0.0% vs 4.2%, p=0.04 for no family history; 5.0% vs 5.9%, p=0.91 for a family history), while reporting a family history affected breast cancer risk for B-13 in whites (4.1% vs 5.9%, p=0.51 for no family history; 0.0% vs 16.7%, p=0.03, family history).

Class II DRB: Findings appeared to be modified by family history for DRB1-09 (0.9% vs 7.4%, p=0.02 for no history; 5.6% vs 5.3%, p=1.00 for positive history), and DRB1-16 (3.5% vs 0.0%, p=0.05 for no history; no prevalence among cases or controls with a history).

Class II DQB: DQB1-05 was marginally associated with breast cancer for black women with a positive family history (46.1% vs 39.7%, p=0.32, no history; 44.4% vs 10.5% p=0.03, family history).

Overall summaries of findings by HLA class type, with consideration of potential impact on incidence rate variation

Class I A summary:

Table 74 shows that A-01, A-11, A-23, A-24, A-32 and A-33 had some association with breast cancer risk, but for most in patterns that differed by race/ethnicity. In the study population combined over racial/ethnic groups, the only allele linked even marginally to breast cancer overall (A-33) had a low prevalence (2.5%), while none of the higher-prevalence alleles (e.g., A-02, A-03) was associated with breast cancer. In data stratified by disease stage, A-01, A-11, A-23, A-30 and A-33 were suggested to impact breast cancer risk irrespective of race/ethnicity but with both increased and reduced risks across alleles for both localized and later-stage disease; most notable were the approximate doubling of risk of localized disease for A-23 and A-33 carriers. A-11 appeared to be a protective factor against ER-positive breast cancer, while A-33 was a strong risk factor for ER-negative disease (based on its impact in black women).

Across racial/ethnic groups, there were marked differences in associations, including some that were consistent with the observed incidence rate differentials. The protective effect of A-01 in Hispanics, in whom the prevalence was relatively high, suggests that this allele may contribute to the reduced breast cancer incidence rate in Hispanics compared to whites and blacks, in whom it is also prevalent but not associated with breast cancer. A-23 may explain some small part of the higher rates of breast cancer in white women, in whom it increased risk for those with localized disease, the majority of cases. Although the prevalence of this allele was low in whites, the higher prevalence of A-23 in blacks in the absence of any disease association could exaggerate the impact of this allele on racial/ethnic differences in breast cancer incidence. A-32 increased risk for black women and reduced risk for Hispanic women. While this allele is unlikely to impact the observed incidence rate patterns strongly, given that it is a rare allele in blacks, the higher prevalence of A-32 in Hispanics in conjunction with the lack of association in whites means that it could contribute in some part to the higher incidence rate for blacks than Hispanics. Other racial/ethnic differences in allele associations were less consistent with observed incidence patterns. A-11 and A-24 were protective alleles for ER-positive breast cancer in whites but not linked to risk in blacks or Hispanics, while A-33 increased risk in black women, particularly the subset defined by having ER-negative tumors. Finally, alleles A-03, A-30, A-31, A-34, A-36, A-66, A-68, and A-74 showed significant inter-racial variation in prevalence in controls but no association with breast cancer.

Class I B summary:

Table 75 shows that B-07, B-13, B-15, B-35, B-39, B-40, B-41, B-45, and B-52 appeared to have some association with breast cancer risk. B-13, B-15, B-39 and B-41 appeared to impact risk for women in all three racial/ethnic groups; B-13 and B-39 were protective factors, while B-15 increased risk predominantly for

localized disease, and B-41 was a stronger risk factor for ER-negative disease. Among these alleles, B-15, B39, B-40, and B-45 had significantly different prevalences in controls across racial/ethnic groups, but none in a gradient consistent with observed incidence differences among the groups.

For B-alleles, race-specific associations with breast cancer that were statistically significant occurred mostly for Hispanic women, and for two of these the associations were protective. B-07 was a protective factor for Hispanic women only; given its relatively high prevalence (8.2%) in this group and the suggestion of associated increased risks for white and black carriers of this allele, B-07 may contribute to the lower breast cancer incidence rates in Hispanics vis a vis the other two groups, particularly given the strong association of B-07 with increased risk of ER-positive disease in black women. B-45 also decreased risk marginally for Hispanic women, although with its relatively low prevalence, it is less likely to contribute substantially to their lower breast cancer incidence rates. Other associations were contradictory to the observed incidence differentials across racial/ethnic groups. B-40 increased risk marginally, and B-41 and B-52 increased risk of ER-negative breast cancer, for Hispanic women. Thus, on balance a contribution of the relatively common B-07 allele to lower incidence rates in Hispanic women would likely be offset to some extent by the opposing directions of the association with B-40, also a common allele, and B-42 and B-52. In addition, alleles B-08, B-42, B-44, B-48, B-53, B-55, B-58, and B-81 showed significant differences in prevalences across racial/ethnic groups but no associations with breast cancer. Together, these patterns reveal complexity in the way HLA class I B genotypes impact incidence patterns, and particularly racial/ethnic variation, at the population level.

Class II DRB1 summary:

Table 76 shows that associations of class II DRB1 alleles were limited to black and Hispanic women, in whom DRB-01, -03, -08, -09, and -16 had some effect on risk. DRB1-01 increased risk of ER-negative disease in black women, while DRB1-03 was protective against localized, and possibly ER-negative, disease in this group; given the frequency of this latter allele in all groups, this protective effect could contribute to the lower rates of breast cancer in blacks than whites. However, the observation that DRB1-08 doubled risk of localized and of ER-negative tumors for Hispanic women is not consistent with incidence rate differentials. Similarly, the suggestion that DRB1-09 was a protective factor for blacks but increased risk of ER-negative disease in Hispanics does not correspond to incidence rate patterns in these two groups. Finally, alleles DRB1-04, -13, -14, and -15 showed significant differences in prevalences across racial/ethnic groups but no associations with breast cancer. Thus, the limitation of any associations of DRB1 alleles with breast cancer to nonwhite women is intriguing, but inconsistent directions of associated risks and the absence of associations in the face of interracial variation in prevalences indicates a complex role of class II genotype to breast cancer incidence differentials across racial/ethnic groups.

Class II DQB1 summary:

Table 77 shows that class II DQB1 alleles also impacted breast cancer risk only in non-white women. DQB1-02 was associated with a reduced risk of ER-negative disease in black women. Given the relatively high prevalence of this allele and the absence of any association for white women, DQB1-02 could contribute in some part to lower incidence in blacks than whites but not to the higher rates in black women than Hispanic women. Similarly, the increased risk of breast cancer for DQB1-05 in blacks (especially for localized disease and ER-negative disease) is inconsistent with white-black incidence differentials although consistent with black-Hispanic incidence differentials. Among Hispanics, the reduced risk for DQB1-05 may contribute to the lower incidence rates in this group, but the increased risks for carriers of DQB1-02 and DQB1-04 are inconsistent with well-described racial/ethnic breast cancer incidence patterns. Thus, as for DRB1, the finding that associations with breast cancer for DQB1 occur only in nonwhite women is notable, but the specific risk patterns cannot easily be interpreted as impacting incidence rate differentials.

Class II DR-DQ haplotype summary:

Across the study population, risk was doubled for women with the DRDQ haplotype 0803, while black women with 0902 were at lower risk of breast cancer. However, the size of the study population did not permit more detailed analyses of the risk patterns for DR-DQ haplotypes by tumor characteristics or family history of breast cancer.

Family history summary:

Family history was of potential interest to our analysis because it is assumed to reflect genetic predisposition. In fact, in our data, associations with some HLA genotypes were modified by self-reported family history of breast cancer. In the small subset of women who reported a family history and thus were presumed to have genetically impacted risk, breast cancer was associated with A-11, B-13 in whites, B-53, and DQB1-05 in black women. For the class I alleles, associations were protective, which is not consistent with the higher risk of breast cancer in familial settings. Among women reporting no family history (the majority of subjects), associations were apparent for A-23, B-27, B-39, B-44, B-45 in Hispanics, B-50, DRB1-09, and DRB1-16; although the numbers of women reporting a family history were small and allele prevalences in this group thus less stable, these differences all suggested an effect limited to the family-history-negative group. However, the fact that some associations increased risk while others decreased risk complicates the interpretation of these results.

The only association that appeared to exhibit an interaction with family history was for A-2 in Hispanics, which was directly associated in women without a family history (57.6% vs 47.2%, p=0.05) but indirectly associated in women with a positive history (30.0% vs 61.1%, p=0.05). However, both associations were only marginally significant.

Discussion:

The occurrence of breast cancer varies considerably by race/ethnicity, especially in post-menopausal women, and much of this variation remains poorly understood[2, 3]. As about 50% of breast cancer patients have no known risk factors[4-6], the search to understand the marked racial/ethnic differences in older women, who have the highest breast cancer rates, needs to include novel factors. The immune system, which is presumed to play an important, if poorly grasped, role in the clearance of malignant cells, is of increasing interest as such a factor. The HLA part of this system appeared promising as a possible contributor to racial/ethnic disparities in breast cancer occurrence, as it has been related to the risk of several diseases including viral cancers (e.g., cervical[7], nasopharyngeal[8, 9], Hodgkin lymphoma[10-12]) and cancers not suspected to have viral etiologies (e.g., lung[13], brain[14], melanoma[15, 16], prostate[17], renal[18], gastric[19, 20]). Moreover, it is coded by highly polymorphic genes that vary extensively across racial/ethnic groups[21, 22]. Yet, HLA genotype has not been well-examined as a risk factor for breast cancer or ever considered as a contributor to racial/ethnic variation for breast cancer. Because an association of HLA with post-menopausal breast cancer, the most common form of the disease, could enhance the understanding of racial/ethnic differences, as well as contribute to characterizing individual risk and developing clinical strategies and novel treatments[23, 24], we explored this possibility in our study.

Our exploratory assessment of HLA associations with breast cancer indicated that HLA genotype is linked to breast cancer risk and, moreover, identified significant racial/ethnic variations in the HLA associations. These patterns support our hypothesis that such differences might contribute to some part of the racial/ethnic variation in breast cancer incidence rates in post-menopausal women (table 78). The increased risk of breast cancer in white women associated with A-23, the protective effects of DRB1-09 and DQB1-05 in black women, and the protective effects of A-01, B-07 and B-45 in Hispanic women are consistent with the corresponding incidence rate differentials noted in these three groups, given their respective population prevalences. Moreover, the relatively high prevalence of the A-01 allele, particularly for Hispanic women, suggests a protective association for this allele that could contribute to the lower incidence rates in this group. However, a relationship of HLA genotype to racial/ethnic difference in breast cancer incidence is likely to be biologically complex, as some alleles increased breast cancer risk only in lower-incidence groups (i.e., A-32 and A-33 for black women; B-40 for Hispanic women) while others demonstrated associations contradictory to observed incidence gradients across racial/ethnic groups. Complexity is further suggested by the modification of associations by breast tumor features and by breast cancer family history, likely also under genetic control to some extent. Without more statistical power for understanding the influence of multiple comparisons on our significance testing, it is also possible that some of our observed associations are due entirely to chance.

Study strengths and limitations

This is the first study to make a systematic examination of the association of HLA class I and class II genotypes based on DNA typing methods with breast cancer in a population-based group of subjects and accounting for population stratification. The study also took into consideration a number of known breast cancer risk factors through restriction to post-menopausal subjects, through stratified analyses to explore interactions with tumor features, and through multivariate modeling to control for reproductive and family history variables in analyses. Nevertheless, it was limited by several factors. First, DNA and interview data were obtained in a previous interview study[1]; while participation was relatively high in the various stages of this study, both interview data and blood samples were obtained for 78.3% of white cases, 76.5% of black cases, and 80.1% of Hispanic cases invited into the study, and 80.0% of white controls, 71.4% of black controls, and 74.8% of Hispanic controls invited into the study. These response rates raise the possibility of bias to study results if nonparticipation in the original study were related to HLA type, as might be the case for HLA correlates of survival in patients[25]. Second, because of the large number of HLA alleles tested for in this study, some of our significant findings likely occurred by chance; if we apply a stringent statistical Bonferroni correction for multiple comparisons, we would not report any significant associations of HLA alleles with breast cancer risk in post-menopausal women. Because this correction is very conservative, and this study is the first to examine this topic in population-based study subjects and using state-of-the-art DNA-based HLA typing, we have chosen to present our uncorrected findings so they may serve as leads for larger studies in the future. A related limitation of our exploratory study is the small sample sizes for rarer alleles and haplotypes, as well as in some study-subject strata, which prevented further examination of interactions in HLA associations (e.g., for breast cancer stratified by both disease stage and ER status) and meaningful multivariate analysis in such groups. In addition, breast cancer family history, which appeared to modify the effect of some allele associations, was based on subject self report without subsequent validation; however, misclassification is unlikely, given findings of high validity for such reports for first- and even second-degree family members[26].

Prior studies:

Despite its limitations, our data contributes substantially to the research addressing risk related to HLA genotype, particularly for post-menopausal women. Table 79 shows that prior studies examining associations based on DNA-based genotyping methods have been limited in number, often focusing on a single HLA class, and either restricted to pre-menopausal women or including a wide age group that thus fails to account for menopausal status, despite its significant impact on risk factor profiles for breast cancer. Four prior studies looked at breast cancer risk associated only with class II DRB and DQB1 alleles typed with DNA methods. Using polymerase chain-reaction (PCR)-sequence-specific oligonucleotide HLA typing, Chaudhuri et al. compared class II distributions for a hospital-based series of 176 white breast cancer patients under age 40 at diagnosis to distributions for a non-random sample of white males and females[27]. After correction for multiple comparisons, protective effects were found for DQB1*03032 (p=0.002, relative risk (RR)=0.04) and DRB1*11 (1101-1104) (p=0.003, RR=0.18), and a deleterious association was detected for DRB3*0201/0202 (55% of patients, 41% of controls, p=0.02). Because DQB1*03032 is not in linkage disequilibrium with either DRB1*11 or DRB3*0201, and because the HLA genes in linkage disequilibrium with DQB1*03032 were not associated with breast cancer, the authors concluded that the DQB1*03032 association with breast cancer is unlikely to be due to linkage disequilibrium. However, subjects were a subset of 850 patients eligible for a separate study, and participation required being alive to give blood[28]; thus, the observed associations could be biased by a second association of HLA with disease aggressiveness or outcome[25]. In addition, the use of male controls may have affected study findings, as the association of HLA with disease can vary by sex[29] and thus affect risk through a sex hormone-based pathway[30, 31], which could be relevant to breast cancer findings. A second study of class II associations using PCR-SSP typing in 36 Iranian breast cancer cases and 36 healthy female controls of unspecified age[32] found breast cancer risk significantly associated with DRB1*12 (50% of patients, 3% of controls, p<0.03). This study failed to find the protective effect for DRB1*11 found in the Chaudhuri data, possibly due to differences in HLA typing methodology, study-population age differences, ethnic differences, or low statistical power[32]. In a third study presented at the XIII International Congress of Histocompatibility and Immunogenetics, Laumbacher and Wank reported breast cancer as significantly associated with class II DQB1*0201 sequencing in 51 patients and 407 controls; allele frequencies differed by sex among the healthy controls, supporting the importance of female controls in breast cancer studies[33]. However, these findings were never published. Finally, Baccar Harrath et al. reported a protective effect of the

class II haplotype DR07-DQ02 in a comparison of 70 Tunisian breast cancer patients ages 27 to 67 at diagnosis in a single institution in 2001 to 70 female blood-donor controls of unspecified age (6.4% vs15.7%, p=0.01 (no correction for multiple comparisons)); the odds ratios estimating breast cancer risk associated with this haplotype was 0.4 (95% CI 0.2 – 0.9), with no mention of adjustment for age or other possible confounders[34].

Two studies included class I alleles. In 2005, Lavado et al. used PCR-SSP on DNA from 132 Spanish breast cancer patients of unspecified age at diagnosis in an unspecified time period and 382 healthy controls in a hospital-based study[35]. Although they found no association with HLA A, DR, DQ or Cw alleles, they did note a significantly increased risk for class I B-07 (p=0.03 after Bonferroni correction; RR=2.1, 95% CI 1.3-3.4); there was no mention of statistical control for potential confounders. Because the cytotoxic function of NK-cells is regulated by HLA class I gene products, Golpalkrishnan et al. compared class I A allele distributions for 81 premenopausal Indian breast cancer patients without any breast cancer family history diagnosed in a single facility to 160 age- and race-matched Indian community controls whose family history was not described[36]. A-11 was more common in patients than controls (18.0% vs 11.3%) but not at a statistically significant level. B-40 (particularly B-4006) also was more common in patients (16.0% vs 9.0%; OR=2.2, 95% CI 1.2 – 4.3), although not at a significant level after adjustment for multiple comparisons.

Thus, to date, published literature based on DNA genotyping has reported breast cancer associations with A-11, B-07, B-40, DRB11, DRB12, DQB02, DQB03 and the DR07-DQ02 haplotype. Although these results were generated across a range of study populations of varying ages and ethnicities and, by and large, from small studies without detailed analyses, some of our findings are similar. Specifically, we have found A-11 to be linked to ER-positive and remote-stage disease, although with risks in an opposite direction to that found by Golpalkrishnan et al[36]. Similarly, we found B-07 to affect risk for black and Hispanic women but again in different directions than reported by Lavado et al[35]. Only the risks for B-40 and DQB1-2 agreed in direction with those reported by others, although in our data the findings were limited to Hispanic women. We did not find the previously noted associations with DRB-11, DRB-12, DQB-3 or the DR07-DQ02 haplotype. Given the strong modification of patterns by race/ethnicity (as anticipated from the differing HLA allele distributions across racial/ethnic groups) as well as by tumor features and breast cancer family history, and, likely, age at diagnosis, this variation in findings is not surprising. However, it points to the importance of population stratification in studies of HLA and disease, including breast cancer, and of the need to consider pre- and post-menopausal breast cancer separately.

Our study findings were summarized for the Era of Hope abstract, poster and platform presentation in Philadelphia, June 8-11, 2005. A manuscript is in preparation.

Key Research Accomplishments:

1) For a population-based series of 915 breast cancer patients and controls, amplified class I (A and B) and class II (DR and DQ) loci, typed using immobilize probe linear arrays, and scanned probe reactivity patterns and convert patterns to genotype.
2) Completed statistical analysis for Class I and II alleles, by comparing allele frequencies for HLA-A, -B, -DRB1, and -DQB1, separately for each race; computing odds ratios and 95% confidence intervals adjusted for age, reproductive factors (age at menarche, at a first full-term pregnancy, duration of lactation) and breast cancer family history; stratifying analyses by tumor characteristics (disease stage at diagnosis, ER status of tumor) and family history of breast cancer; and comparing across racial/ethnic groups those HLA associations significant in any racial/ethnic group.

Reportable Outcomes:

1) Abstract (Bugawan TL et al.) accepted for poster presentation at the American Society of Histocompatibility and Immunogenetics meeting, October, 2005
2) Abstract (Glaser SL et al.) as required for Era of Hope meeting, June 8-11, 2005, Philadelphia
3) Poster as required for Era of Hope meeting, June 8-11, 2005, Philadelphia
4) Invited platform presentation, Era of Hope meeting, June 9, 2005, Philadelphia

Conclusions:

This first in-depth exploration of the relation of HLA genotype to breast cancer in race-specific populations has showed that HLA genotype appears to be related to breast cancer in population-representative post-menopausal white, black and Hispanic women. Overall, breast cancer risk was suggestively increased for women with class I A-33 and suggestively decreased for women with class I B-13 or B-39. There were no significant associations for breast cancer overall with class II DRB1 or DQB1 alleles, although the DR-DQ haplotype 0803 was associated with a doubling of breast cancer risk. However, these HLA-associated risks appeared to be modified by tumor characteristics, with some associations limited to localized or regional/remote disease, or ER-positive or –negative tumors, and by family history, another genetically impacted characteristic.

Our data also showed that the association of HLA genotype with breast cancer differed across racial/ethnic group. For white women, those with A-23 were at increased risk of breast cancer overall, while those with A-11 or A-24 were at decreased risk of ER-positive disease. For black women, breast cancer risk was more impacted by HLA type. Black women with A-32, A-33 and DQB-5 were at increased or marginally increased breast cancer risk, while those with DRB-9 were at reduced risk. For Hispanic women, breast cancer risk was lower for those positive for A-01, B-07, and B-45, but elevated for those with B-40. Some of these associations were also modified by disease stage and ER status of tumors, and by family history of breast cancer with some risks stronger in or confined to specific strata of these characteristics. Associations noted for A-01, A-23, A-32, B-07, DRB1-01, DQB1-02 and DQB1-05 are consistent with observed incidence differentials across racial/ethnic groups, although all other associations were in directions contradictory to these patterns.

We conclude that a variety of HLA Class I and II alleles appears to be related to breast cancer risk in post-menopausal women, with apparent differences in associations by race/ethnicity and modifications by tumor characteristics and family history. Our findings do support a possible role of HLA or linked loci in contributing to breast cancer occurrence and, in some part, to racial/ethnic variation in breast cancer incidence. In theory, specific HLA class II molecules might play a part in immunosurveillance of breast cancer through effects of T-helper cell cytotoxicity, cytokine secretion, or function of T-helper cells[32], and thus HLA may be involved in immunosurveillance and/or hormonal pathways related to breast cancer. However, the complexities of the associations we noted indicated that the relationship of HLA type to breast cancer incidence may be biologically complicated, particularly as regards the incidence differential across racial/ethnic groups. Our findings are novel, in that they report associations of breast cancer with aspects of immune function, whose role in breast cancer development is logical but little investigated to date. Given their positive nature, our findings support further basic and epidemiologic research into the impact of HLA on breast cancer development. However, the extensive polymorphism of HLA will require that this work be undertaken in a study population large enough to overcome the limits of multiple comparisons and also to permit the evaluation of associations in subgroups of breast cancer defined by stage and ER status, shown by others to describe distinctive forms of this cancer[37].

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Table 1. Distributions of breast cancer cases and community controls by demographic and tumor characteristics, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

Factor	White				Black				Hispanic			
	Cases		Controls		Cases		Controls		Cases		Controls	
	n	%	n	%	n	%	n	%	n	%	n	%
Age at diagnosis												
40-44	1	0.7	1	0.6	0	0.0	2	1.4	2	1.4	3	1.6
45-49	7	4.6	3	1.9	12	9.0	11	7.9	6	4.3	5	2.7
50-54	9	5.9	6	3.7	25	18.7	18	12.9	17	12.1	30	16.0
55-50	29	19.1	29	17.9	23	17.2	27	19.3	37	26.4	47	25.1
60-64	22	14.5	23	14.2	24	17.9	23	16.4	30	21.4	36	19.3
65-69	26	17.1	30	18.5	15	11.2	24	17.1	16	11.4	32	17.1
70-74	30	19.7	34	21.0	16	11.9	21	15.0	18	12.9	25	13.4
75-79	27	17.8	35	21.6	19	14.2	13	9.3	13	9.3	9	4.8
80+	1	0.7	1	0.6	0	0.0	1	0.7	1	0.7	0	0.0
Age at menarche*												
<12	31	20.8	33	20.5	25	18.8	27	19.3	41	29.3	35	18.9
>=12	118	79.2	128	79.5	108	81.2	113	80.7	99	70.7	150	81.1
Parity**												
Nulliparous	24	15.8	34	21.0	28	20.9	13	9.3	16	11.4	13	7.0
Parous	128	84.2	128	79.0	106	79.1	127	90.7	124	88.6	174	93.0
Age at first birth (among the parous)												
<30	19	14.8	18	14.1	12	11.3	8	6.3	21	16.9	21	12.1
30+	109	85.2	110	85.9	94	88.7	119	93.7	103	83.1	153	87.9
Duration of lactation (among the parous)												
<5 months	82	64.1	81	63.3	67	63.2	88	69.3	75	60.5	88	50.6
>=5 months	46	35.9	47	36.7	39	36.8	39	30.7	49	39.5	86	49.4
Breast cancer family history (self-reported)												
No	122	80.3	138	85.2	115	85.8	121	86.4	120	85.7	169	90.4
Yes	30	19.7	24	14.8	19	14.2	19	13.6	20	14.3	18	9.6
Disease stage at diagnosis												
Localized	119	78.3	N/A		98	74.2	N/A		98	70.5	N/A	
Regl/remote	33	21.7	N/A		34	25.8	N/A		41	29.5	N/A	
Tumor ER status												
ER-positive	117	77.0	N/A		70	52.2	N/A		96	68.6	N/A	
ER-negative	14	9.2	N/A		37	27.6	N/A		24	17.1	N/A	
Unknown	21	13.8	N/A		27	20.1	N/A		20	14.3	N/A	

* p-value for case-control difference=0.03 in Hispanics
**p-value for case-control difference=0.01 in blacks

Table 2. Relative frequencies of HLA **Class I A** allele distributions by allele and breast cancer case-control status, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	Cases N=846	Controls N=966	p*
A-01	9.2	9.8	0.66
A-02	26.4	26.3	0.97
A-03	10.4	9.1	0.35
A-11	3.6	5.0	0.14
A-23	**5.2**	**3.3**	**0.05**
A-24	7.2	9.2	0.12
A-25	0.8	1.1	0.51
A-26	2.5	2.9	0.60
A-29	4.6	3.4	0.19
A-30	6.3	6.3	0.97
A-31	3.6	3.0	0.52
A-32	2.7	2.8	0.92
A-33	3.8	2.5	0.11
A-34	1.9	1.5	0.46
A-36	0.6	0.5	1.00
A-66	1.3	1.4	0.93
A-68	8.3	8.8	0.69
A-69	-	0.1	1.00
A-74	1.7	2.8	0.10
A-80	0.1	0.2	1.00

* chi-square or Fisher's exact test

Table 3. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA class I A alleles most strongly with breast cancer risk in any racial/ethnic group, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	All women	
	OR*	95% CI
A-01	0.9	0.6 – 1.2
A-11	0.7	0.4 – 1.2
A-23	1.5	0.9 – 2.5
A-24	0.8	0.6 – 1.2
A-25	0.6	0.2 – 1.7
A-29	1.3	0.8 – 2.7
A-31	1.3	0.7 – 2.2
A-32	0.9	0.5 – 1.6
A-33	**1.8**	**1.0 – 3.2**
A-66	0.8	0.4 – 1.9
A-68	0.9	0.6 – 1.3
A-74	0.6	0.3 – 1.2

* adjusted for age at diagnosis, race/ethnicity, age at menarche, age at first birth, duration of lactation, family history of breast cancer

Table 4. Relative frequencies of HLA **Class I A** allele distributions by allele, breast cancer case-control status, and racial/ethnic group, post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	Whites			Blacks			Hispanics		
	Cases N=304	Controls N=318	p*	Cases N=266	Controls N=280	p*	Cases N=276	Controls N=368	p*
A-01	15.5	13.2	0.42	5.3	5.7	0.82	6.2	10.1	0.08
A-02	27.3	27.7	0.92	20.7	21.4	0.83	30.8	28.8	0.58
A-03	15.5	13.2	0.42	6.4	6.1	0.90	8.7	7.9	0.71
A-11	5.6	8.2	0.20	1.5	1.4	1.00	3.3	4.9	0.31
A-23	**4.0**	**0.9**	**0.01**	9.0	8.2	0.74	2.9	1.6	0.27
A-24	5.6	9.4	0.07	2.6	3.6	0.53	13.4	13.3	0.97
A-25	2.0	1.9	0.94	-	0.7	0.50	0.4	0.8	0.64
A-26	2.6	3.1	0.70	1.9	3.2	0.32	2.9	2.5	0.72
A-29	3.6	4.1	0.76	5.3	3.2	0.23	5.1	3.0	0.18
A-30	3.6	2.8	0.58	10.2	13.9	0.18	5.4	3.5	0.24
A-31	4.0	2.2	0.21	0.8	1.1	1.00	5.8	5.2	0.73
A-32	3.3	4.7	0.36	**3.8**	**0.4**	**0.005**	1.1	3.0	0.10
A-33	2.0	1.3	0.54	6.8	4.3	0.20	2.9	2.2	0.56
A-34	-	0.3	1.00	6.0	4.6	0.50	-	-	
A-36	-	-		1.9	1.8	1.00	-	-	
A-66	-	0.6	0.50	3.4	3.2	0.91	0.7	0.5	1.00
A-68	4.9	4.7	0.90	10.5	8.9	0.53	9.8	12.2	0.33
A-69	-	-		-	-		-	0.3	1.00
A-74	0.7	1.6	0.45	3.8	7.5	0.06	0.7	0.3	0.58
A-80	-	-		0.4	0.7	1.00	-	-	

* chi-square or Fisher's exact test

Table 5. Adjusted* odds ratios and 95% confidence intervals for associations of the strongly associated HLA **class I A** alleles with breast cancer risk by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
A-01	*13.2*	1.2	0.7 – 2.0	*5.7*	1.0	0.5 – 2.2	***10.1***	**0.5**	**0.3 – 0.98**
A-11	*8.2*	0.7	0.3 – 1.3	*1.4*	1.4	0.3 – 6.0	*4.9*	0.7	0.3 – 1.6
A-23	***0.9***	**4.0**	**1.1 –15.0**	*8.2*	1.1	0.6 – 2.1	*1.6*	1.6	0.5 – 4.9
A-24	*9.4*	0.6	0.3 – 1.2	*3.6*	0.6	0.2 – 1.8	*13.3*	1.0	0.6 – 1.7
A-25	*1.9*	1.0	0.3 – 3.4	*0.7*	***		*0.8*	0.5	0.1 – 5.2
A-29	*4.1*	0.9	0.4 – 2.0	*3.2*	1.7	0.7 – 4.2	*3.0*	1.4	0.6 – 3.2
A-31	*2.2*	1.5	0.5 – 4.1	*1.1*	0.6	0.1 – 4.1	*5.2*	1.3	0.6 – 2.7
A-32	*4.7*	0.7	0.3 – 1.6	***0.4***	**10.0**	**1.2 – 82.5**	*3.0*	0.3	0.1 – 1.1
A-33	*1.3*	1.5	0.4 – 5.5	*4.3*	2.4	1.0 – 5.6	*2.2*	1.7	0.6 – 4.9
A-66	*0.6*	***		*3.2*	1.1	0.4 – 2.9	*0.5*	1.3	0.2 – 9.6
A-68	*4.7*	0.9	0.4 – 2.0	*8.9*	0.9	0.5 – 1.8	*12.2*	0.8	0.4 – 1.4
A-74	*1.6*	0.5	0.1 – 2.7	*7.5*	0.5	0.2 – 1.1	*0.3*	2.3	0.2 – 27.4

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 6. Relative frequencies of HLA **Class I B** allele distributions by allele and breast cancer case-control status, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	Cases N=848	Controls N=968	p*
B-07	9.9	8.6	0.33
B-08	6.3	5.9	0.75
B-13	**1.2**	**2.6**	**0.03**
B-14	3.5	3.6	0.93
B-15	9.6	7.3	0.09
B-18	4.0	3.5	0.58
B-27	2.4	3.5	0.15
B-35	10.3	10.6	0.79
B-37	0.6	1.0	0.30
B-38	1.2	1.8	0.31
B-39	**2.6**	**4.8**	**0.02**
B-40	7.4	6.3	0.34
B-41	1.1	0.6	0.30
B-42	1.6	2.4	0.28
B-44	12.0	9.7	0.11
B-45	1.7	2.5	0.22
B-47	0.4	0.5	0.73
B-48	0.9	0.9	0.98
B-49	2.5	2.2	0.66
B-50	**0.8**	**2.0**	**0.04**
B-51	5.3	4.4	0.39
B-52	1.9	1.8	0.84
B-53	4.3	5.2	0.36
B-54	0.1	-	0.47
B-55	1.3	0.9	0.45
B-56	0.1	0.6	0.13
B-57	2.2	3.3	0.17
B-58	3.5	2.4	0.14
B-73	0.1	-	0.47
B-78	0.7	0.4	0.53
B-81	0.5	0.4	1.00
B-82	0.1	0.3	0.63

* chi-square or Fisher's exact test

Table 7. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class I B** alleles most strongly with breast cancer risk in any racial/ethnic group, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	All women	
	OR*	95% CI
B-07	1.1	0.8 – 1.6
B-13	**0.5**	**0.2 – 0.99**
B-15	1.3	0.9 – 1.9
B-37	0.6	0.2 – 1.9
B-39	**0.6**	**0.3 – 0.99**
B-40	1.3	0.9 – 2.0
B-42	0.7	0.3 – 1.4
B-44	1.2	0.9 – 1.7
B-45	0.6	0.3 – 1.2
B-50	0.4	0.2 – 1.1
B-56	0.2	0.02 –1.6
B-57	0.6	0.4 – 1.2

* adjusted for age at diagnosis, race/ethnicity, age at menarche, age at first birth, duration of lactation, family history of breast cancer

Table 8. Relative frequencies of HLA **Class I B** allele distributions by allele, breast cancer case-control status, and racial/ethnic group, post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	Whites			Blacks			Hispanics		
	Cases N=304	Controls N=320	p*	Cases N=266	Controls N=280	p*	Cases N=278	Controls N=368	p*
B-07	14.8	10.9	0.15	10.2	6.4	0.11	**4.3**	**8.2**	**0.05**
B-08	10.9	10.6	0.93	3.4	2.9	0.72	4.0	4.1	0.94
B-13	1.6	3.8	0.11	0.8	1.8	0.45	1.1	2.2	0.37
B-14	4.0	3.8	0.90	3.4	2.5	0.54	3.2	4.4	0.47
B-15	7.6	5.6	0.33	13.2	12.1	0.72	8.3	5.2	0.11
B-18	2.6	2.8	0.89	4.9	4.6	0.89	4.7	3.3	0.36
B-27	3.3	4.4	0.48	1.1	2.1	0.51	2.5	3.8	0.36
B-35	7.9	10.6	0.24	5.3	7.1	0.36	17.6	13.3	0.13
B-37	-	0.9	0.25	0.8	0.7	1.00	1.1	1.4	1.00
B-38	1.3	1.6	1.00	0.4	1.1	0.62	1.8	2.5	0.58
B-39	1.0	3.1	0.06	1.5	1.1	0.72	5.4	9.0	0.09
B-40	6.6	6.6	0.99	1.9	2.1	0.83	13.7	9.2	0.08
B-41	1.0	0.3	0.36	0.8	1.1	1.00	1.4	0.5	0.41
B-42	-	-		4.1	7.1	0.13	1.1	0.8	1.00
B-44	16.8	15.6	0.70	**12.4**	**7.1**	**0.04**	6.5	6.5	0.98
B-45	0.7	0.6	1.00	4.1	5.0	0.63	0.4	2.2	0.09
B-47	-	0.3	1.00	0.4	-	0.49	0.7	1.1	0.70
B-48	0.3	-	0.49	-	-		2.5	2.5	0.95
B-49	2.6	1.3	0.21	2.3	2.1	0.93	2.5	3.0	0.72
B-50	0.7	1.9	0.29	0.4	1.8	0.22	1.4	2.2	0.49
B-51	7.2	5.3	0.32	3.4	2.1	0.38	5.0	5.4	0.82
B-52	1.0	1.6	0.73	0.8	1.8	0.45	4.0	1.9	0.12
B-53	1.3	1.6	1.00	9.8	11.8	0.45	2.2	3.3	0.40
B-54	0.3	-	0.49	-	-		-	-	
B-55	2.6	2.2	0.72	0.8	0.7	1.00	0.4	-	0.43
B-56	0.3	0.9	0.62	-	-		-	0.8	0.26
B-57	2.6	3.1	0.71	3.0	5.0	0.24	1.1	2.2	0.37
B-58	1.0	0.6	0.68	8.3	6.4	0.41	1.8	0.8	0.30
B-73	-	-		-	-		0.4	-	0.43
B-78	-	-		1.5	1.1	0.72	0.7	0.3	0.58
B-81	-	-		1.1	1.4	1.00	0.4	-	0.43
B-82	-	-		0.4	0.7	1.00	-	0.3	1.00

* chi-square or Fisher's exact test

Table 9. Adjusted* odds ratios and 95% confidence intervals for associations of the strongly associated HLA **class I B** alleles with breast cancer risk by race/ethnicity, post-menopausal women, Greater Bay Area

HLA-B allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**
B-07	*10.9*	1.3	0.8 – 2.3	*6.4*	1.8	0.9 – 3.5	***8.2***	**0.5**	**0.2 – 0.96**
B-13	*3.8*	0.4	0.1 – 1.2	*1.8*	0.4	0.1 – 2.4	*2.2*	0.6	0.1 – 2.5
B-15	*5.6*	1.4	0.7 – 2.8	*12.1*	1.0	0.5 – 1.7	*5.2*	1.8	0.9 – 3.6
B-37	*0.9*	***		*0.7*	1.1	0.1 – 9.0	*1.4*	0.8	0.2 – 3.9
B-39	*3.1*	0.4	0.1 – 1.6	*1.1*	1.2	0.3 – 5.9	*9.0*	0.5	0.3 – 1.1
B-40	*6.6*	1.2	0.6 – 2.3	*2.1*	1.0	0.3 – 3.4	***9.2***	**1.8**	**1.0 – 3.1**
B-42	--	--		*7.1*	0.6	0.3 – 1.3	*0.8*	1.6	0.3 – 8.3
B-44	*15.6*	1.2	0.7 – 1.9	*7.1*	1.7	0.9 – 3.3	*6.5*	0.9	0.4 – 1.8
B-45	*0.6*	1.0	0.1 – 7.4	*5.0*	0.7	0.3 – 1.6	***2.2***	**0.1**	**0.01 – 1.0**
B-50	*1.9*	0.4	0.1 – 1.8	*1.8*	0.3	0.03 – 2.3	*2.2*	0.9	0.3 – 3.2
B-56	*0.9*	0.4	0.03 – 3.6	--	--		*0.8*	***	
B-57	*3.1*	0.8	0.3 – 2.2	*5.0*	0.5	0.2 – 1.3	*2.2*	0.4	0.1 – 1.7

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 10. Relative frequencies of HLA **Class II DRB-1** allele distributions by allele and breast cancer case-control status, all post-menopausal women, Greater Bay Area, 1997-1999

HLA DRB-1 allele	Cases	Controls	p*
	N=840	N=958	
DRB-01	8.8	8.5	0.79
DRB-03	10.5	9.9	0.70
DRB-04	14.6	16.6	0.26
DRB-07	11.2	10.2	0.51
DRB-08	7.6	6.5	0.34
DRB-09	1.2	1.3	0.90
DRB-10	0.6	1.0	0.30
DRB-11	9.8	9.4	0.79
DRB-12	2.3	2.2	0.92
DRB-13	14.2	13.5	0.67
DRB-14	5.6	5.7	0.89
DRB-15	12.0	13.7	0.30
DRB-16	1.7	1.6	0.87

* chi-square or Fisher's exact test

Table 11. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DRB-1** alleles most strongly with breast cancer risk in any racial/ethnic group, all post-menopausal women, Greater Bay Area

HLA-DRB-1 allele	All women	
	OR*	95% CI
DRB1-01	1.0	0.7 – 1.5
DRB1-03	1.0	0.7 – 1.4
DRB1-04	0.9	0.6 – 1.2
DRB1-07	1.2	0.8 – 1.6
DRB1-08	1.3	0.8 – 2.0
DRB1-09	1.0	0.4 – 2.3
DRB1-10	0.6	0.2 – 1.8
DRB1-12	1.0	0.5 – 1.9
DRB1-13	1.0	0.7 – 1.4
DRB1-15	0.9	0.6 – 1.2
DRB1-16	1.1	0.5 – 2.3

* adjusted for age at diagnosis, race/ethnicity, age at menarche, age at first birth, duration of lactation, family history of breast cancer

Table 12. Relative frequencies of HLA **Class II DRB-1 allele** distributions by allele, breast cancer case-control status, and racial/ethnic group, post-menopausal women, Greater Bay Area, 1997-1999

HLA DRB-1 allele	Whites			Blacks			Hispanics		
	Cases	Controls	p*	Cases	Controls	p*	Cases	Controls	p*
	N=298	N=312		N=266	N=280		N=276	N=366	
DRB-01	11.1	10.3	0.74	8.3	5.4	0.18	6.9	9.3	0.27
DRB-03	12.4	10.9	0.56	9.0	13.2	0.12	9.8	6.6	0.13
DRB-04	15.4	18.6	0.30	5.6	4.3	0.47	22.5	24.3	0.58
DRB-07	14.4	12.5	0.48	9.8	9.6	0.96	9.1	8.7	0.89
DRB-08	3.0	4.5	0.34	8.7	6.4	0.33	11.6	8.2	0.15
DRB-09	1.3	0.3	0.21	**0.8**	**3.6**	**0.02**	1.5	0.3	0.17
DRB-10	-	0.3	1.00	1.1	1.4	1.00	0.7	1.4	0.70
DRB-11	9.4	9.6	0.93	10.9	11.1	0.95	9.1	7.9	0.61
DRB-12	0.7	1.6	0.45	6.0	3.6	0.18	0.4	1.6	0.25
DRB-13	14.4	10.6	0.15	19.9	20.7	0.82	8.3	10.4	0.38
DRB-14	3.4	3.2	0.92	3.8	2.9	0.56	9.8	10.1	0.89
DRB-15	12.4	15.7	0.24	14.7	17.9	0.31	9.1	8.7	0.89
DRB-16	2.0	1.9	0.94	1.5	-	0.06	1.5	2.5	0.37

* chi-square or Fisher's exact test

Table 13. Adjusted* odds ratios and 95% confidence intervals for associations of the strongly associated HLA **class II DRB-1** alleles with breast cancer risk by race/ethnicity, post-menopausal women, Greater Bay Area

HLA-DRB-1 allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**
DRB1-01	*10.3*	0.9	0.5 – 1.6	*5.4*	1.7	0.8 – 3.5	*9.3*	0.7	0.4 – 1.4
DRB1-03	*10.9*	1.1	0.6 – 2.0	*13.2*	0.7	0.4 – 1.2	*6.6*	1.5	0.8 – 2.9
DRB1-04	*18.6*	0.7	0.5 – 1.2	*4.3*	1.4	0.6 – 3.3	*24.3*	1.0	0.6 – 1.5
DRB1-07	*12.5*	1.3	0.8 – 2.2	*9.6*	1.0	0.5 – 1.9	*8.7*	1.0	0.6 – 1.9
DRB1-08	*4.5*	0.7	0.3 – 1.6	*6.4*	1.5	0.7 – 3.1	*8.2*	1.6	0.9 – 3.0
DRB1-09	*0.3*	4.3	0.5 –38.5	***3.6***	**0.2**	**0.04 –0.8**	*0.3*	5.7	0.6 – 53.5
DRB1-12	*1.6*	0.4	0.1 – 2.2	*3.6*	1.8	0.8 – 4.1	*0.4*	0.2	0.02 – 1.6
DRB1-13	*10.6*	1.5	0.8 – 2.5	*20.7*	1.0	0.6 – 1.7	*8.3*	0.7	0.4 – 1.3
DRB1-16	*1.9*	1.0	0.3 – 3.2	--	***		*2.5*	0.6	0.2 – 2.0

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 14. Relative frequencies of HLA **Class II DQB-1** allele distributions by allele and breast cancer case-control status, all post-menopausal women, Greater Bay Area, 1997-1999

HLA DQB-1 allele	Cases	Controls	p*
	N=850	N=964	
DQB1-02	20.2	18.2	0.26
DQB1-03	32.9	35.4	0.28
DQB1-04	6.7	6.9	0.91
DQB1-05	17.7	16.3	0.44
DQB1-06	22.5	23.3	0.66

* chi-square or Fisher's exact test

Table 15. Adjusted* odds ratios and 95% confidence intervals for associations of HLA **class II DQB-1** alleles with breast cancer risk in any racial/ethnic group, all post-menopausal women, Greater Bay Area

HLA DQB-1 allele	All women	
	OR*	95% CI
DQB1-02	1.1	0.8 – 1.5
DQB1-03	0.9	0.7 – 1.2
DQB1-04	1.1	0.7 – 1.6
DQB1-05	1.1	0.8 – 1.4
DQB1-06	0.9	0.7 – 1.2

* adjusted for age at diagnosis, race/ethnicity, age at menarche, age at first birth, duration of lactation, family history of breast cancer

Table 16. Relative frequencies of HLA **Class II DQB-1** allele distributions by allele, breast cancer case-control status, and racial/ethnic group, post-menopausal women, Greater Bay Area, 1997-1999

HLA DQB-1 Allele	Whites			Blacks			Hispanics		
	Cases N=304	Controls N=314	p*	Cases N=266	Controls N=280	p*	Cases N=280	Controls N=370	p*
DQB1-02	23.0	20.1	0.37	18.4	22.5	0.24	**18.9**	**13.2**	**0.05**
DQB1-03	31.3	35.0	0.32	25.2	21.8	0.35	42.1	46.0	0.33
DQB1-04	3.3	4.1	0.58	4.1	6.4	0.23	12.9	9.5	0.17
DQB1-05	17.4	15.6	0.54	24.8	18.9	0.10	11.1	14.9	0.16
DQB1-06	25.0	25.2	0.96	27.4	30.4	0.45	15.0	16.5	0.61

* chi-square or Fisher's exact test

Table 17. Adjusted* odds ratios and 95% confidence intervals for associations of HLA **class II DQB-1** alleles with breast cancer risk by race/ethnicity, post-menopausal women, Greater Bay Area

HLA-DQB-1 allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**
DQB1-02	*20.1*	1.1	0.7 – 1.8	*22.5*	0.8	0.5 – 1.3	*13.2*	1.5	0.9 – 2.4
DQB1-03	*35.0*	0.8	0.5 – 1.3	*21.8*	1.1	0.7 – 1.9	*46.0*	1.0	0.6 – 1.6
DQB1-04	*4.1*	0.9	0.4 – 2.1	*6.4*	0.7	0.3 – 1.5	*9.5*	1.6	0.9 – 2.8
DQB1-05	*15.6*	1.0	0.6 – 1.7	*18.9*	**1.6**	**0.97 –2.6**	*14.9*	0.7	0.4 – 1.2
DQB1-06	*25.2*	1.1	0.7 – 1.7	*30.4*	0.8	0.5 – 1.3	*16.5*	0.9	0.5 – 1.4

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 18. Relative frequencies of HLA **Class II DR-DQ haplotype** distributions by haplotypes and breast cancer case-control status, all post-menopausal women, Greater Bay Area, 1997-1999

HLA DR-DQ haplotype	Cases	Controls	p*
	N=840	N=954	
0102	0.1	-	0.47
0103	0.1	0.1	1.00
0105	8.6	8.4	0.89
0302	9.2	8.1	0.41
0303	0.1	-	0.47
0304	1.1	1.8	0.21
0305	-	0.1	1.00
0306	0.1	-	0.47
0402	0.4	0	0.10
0403	13.3	16.0	0.11
0404	0.7	0.4	0.53
0405	0.2	0.1	0.60
0702	9.2	8.2	0.46
0703	1.7	2.1	0.51
0704	0.1	-	0.47
0705	0.2	-	0.21
0803	**3.0**	**1.5**	**0.03**
0804	4.3	4.2	0.92
0805	-	0.4	0.13
0806	0.4	0.4	1.00
0902	0.4	0.9	0.15
0903	0.8	0.3	0.20
1005	0.6	1.1	0.31
1102	0.1	-	0.47
1103	7.4	8.0	0.64
1104	0.2	0.1	0.60
1105	0.5	0.4	1.00
1106	1.6	0.7	0.10
1203	0.6	1.2	0.21
1205	1.7	0.8	0.11
1302	1.0	0.7	0.61
1303	3.1	2.5	0.46
1304	0.1	-	0.47
1305	1.2	1.7	0.39
1306	8.8	8.6	0.87
1402	-	0.1	1.00
1403	2.3	2.9	0.37
1404	0.2	0.2	1.00
1405	3.0	2.3	0.38
1406	0.1	0.1	1.00
1502	0.2	0.1	0.60
1503	-	0.2	0.50
1505	0.4	0.2	0.67
1506	11.4	13.2	0.25
1603	0.6	0.6	0.93
1604	-	0.2	0.50
1605	1.0	0.6	0.44
1606	0.1	0.1	1.00

***** chi-square or Fisher's exact test

Table 19. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DRDQ haplotypes** most strongly with breast cancer risk in any racial/ethnic group, all post-menopausal women, Greater Bay Area

HLA-DRDQ haplotypes	All women	
	OR*	95% CI
DRDQ-0402	**	
DRDQ-0403	0.8	0.6 – 1.1
DRDQ-0404	1.9	0.5 – 7.0
DRDQ-0405	2.8	0.2 – 31.3
DRDQ-0705	**	
DRDQ-0803	**2.2**	**1.1 – 4.5**
DRDQ-0805	**	
DRDQ-0902	0.3	0.1 – 1.3
DRDQ-1104	2.2	0.2 – 24.7
DRDQ-1105	1.1	0.3 – 4.4
DRDQ-1106	2.1	0.8 – 5.4
DRDQ-1203	0.5	0.2 – 1.5
DRDQ-1205	1.9	0.8 – 4.8
DRDQ-1305	0.7	0.3 – 1.6
DRDQ-1503	**	
DRDQ-1603	1.1	0.3 – 3.6

* adjusted for age at diagnosis, race/ethnicity, age at menarche, age at first birth, duration of lactation, family history of breast cancer

** unstable model

Table 20. Relative frequencies of HLA **Class II DR-DQ haplotype** distributions by haplotype, breast cancer case-control status, and racial/ethnic group, post-menopausal women, Greater Bay Area, 1997-1999

HLA DR-DQ haplotype	Whites			Blacks			Hispanics		
	Cases N=298	Controls N=310	p*	Cases N=266	Controls N=280	p*	Cases N=276	Controls N=364	p*
0102	0.3	-	0.49	-	-		-	-	
0103	0.3	0.3	1.00	-	-		-	-	
0105	10.4	10.0	0.87	8.3	5.4	0.18	6.9	9.3	0.26
0302	12.1	11.0	0.67	6.0	7.5	0.49	9.1	6.0	0.15
0303	0.3	-	0.49	-	-		-	-	
0304	-	-		3.0	5.4	0.17	0.4	0.6	1.00
0305	-	-		-	0.4	1.00	-	-	
0306	-	-		-	-		0.4	-	0.43
0402	0.3	-	0.49	-	-		0.7	-	0.19
0403	14.1	18.7	0.12	4.9	3.9	0.58	20.7	23.1	0.46
0404	1.0	-	0.12	-	0.4	1.00	1.1	0.8	1.00
0405	-	-		0.8	-	0.24	-	0.3	1.00
0702	10.7	9.0	0.48	8.3	9.3	0.68	8.3	6.6	0.40
0703	3.7	3.6	0.92	0.4	0.4	1.00	0.7	2.2	0.20
0704	-	-		0.4	-	0.49	-	-	
0705	-	-		0.8	-	0.24	-	-	
0803	0.7	0.3	0.62	7.1	3.9	0.10	1.5	0.6	0.41
0804	2.4	3.2	0.51	0.8	0.7	1.00	9.8	7.7	0.35
0805		0.7	0.50	-	0.7	0.50	-	-	
0806		0.3	1.00	0.8	1.1	1.00	0.4	0	0.43
0902	-	-		**0.8**	**3.2**	**0.04**	0.4	0	0.25
0903	1.3	0.3	0.21	-	0.4	1.00	1.1	0.3	0.32
1005		0.3	1.00	1.1	1.4	1.00	0.7	1.4	0.71
1006	-	-		-	-		-	-	
1102	-	-		0.4	-	0.49	-	-	
1103	8.4	9.0	0.78	5.6	7.9	0.30	8.0	7.1	0.69
1104		0.3	1.00	-	-		0.7	-	0.19
1105	0.3		0.49	1.1	1.1	1.00	0	0.3	1.00
1106	0.7		0.24	3.8	2.1	0.26	0.4	0.3	1.00
1203	0.7	1.0	1.00	0.8	1.1	1.00	0.4	1.4	0.24
1205	-	-		5.3	2.5	0.09	-	0.3	1.00
1302	-	-		2.6	2.1	0.71	0.4	0.3	1.00
1303	1.7	1.9	0.81	5.3	3.6	0.34	2.5	2.2	0.78
1304	-	-		-	-		0.4	-	0.51
1305	0.3		0.49	3.4	5.0	0.35	-	0.6	0.22
1306	12.4	8.7	0.14	8.7	10.0	0.59	5.1	7.4	0.23
1402	-	-		-	-		-	0.3	1.00
1403	-	-		0.4	0.7	1.00	6.5	7.1	0.76
1404	-	-		-	-		0.7	0.6	1.00
1405	3.4	2.9	0.75	3.0	2.1	0.52	2.5	1.9	0.60
1406	-	-		0.4	-	0.49	-	0.3	1.00
1502	-	-		0.4	0.4	1.00	0.4	-	0.43
1503	-	-		-	-		-	0.6	0.51
1505	0.7		0.15	0.4	0.4	1.00	-	0.3	1.00
1506	11.7	15.8	0.24	13.9	17.1	0.30	8.7	8.0	0.74
1603	-	-		0.8	-	0.24	1.1	1.7	0.74
1604		0.7	0.50	-	-		-	-	
1605	1.7	1.3	0.75	0.8		0.24	0.4	0.6	1.00
1606	0.3		0.49	-	-		-	0.3	1.00

Table 21. Adjusted* odds ratios and 95% confidence intervals for associations of the strongly associated HLA **class II DRDQ haplotypes** with breast cancer risk by race/ethnicity, post-menopausal women, Greater Bay Area

HLA-DRDQ haplotypes	Whites		Blacks		Hispanics	
	OR*	95% CI	OR*	95% CI	OR*	95% CI
DRDQ-0402	**		1.1	0.5 – 2.2	**	
DRDQ-0403	0.7	0.4 – 1.1	1.3	0.5 – 3.2	0.9	0.6 – 1.4
DRDQ-0404	**		**		1.6	0.3 – 8.5
DRDQ-0405	--		**		**	
DRDQ-0705	--		**		--	
DRDQ-0803	2.0	0.2 – 23.3	2.1	0.9 – 4.7	2.8	0.5 – 16.6
DRDQ-0805	**		**		--	
DRDQ-0902	--		**0.2**	**0.04 – 0.9**	**	
DRDQ-1104	**		1.1	0.5 – 2.2	**	
DRDQ-1105	**		0.8	0.1 – 4.1	**	
DRDQ-1106	**		1.8	0.6 – 5.2	1.2	0.1 – 20.3
DRDQ-1203	0.7	0.1 – 4.3	0.8	0.1 – 4.7	0.2	0.02 – 2.1
DRDQ-1205	--		2.2	0.8 – 5.7	**	
DRDQ-1305	--		0.8	0.3 – 1.9	**	
DRDQ-1503	--		1.1	0.5 – 2.2	**	
DRDQ-1603	--		**		0.6	0.1 – 2.9
DRDQ-1605	1.2	0.3 – 4.9	**		0.6	0.1 – 7.3

* adjusted for age at diagnosis, race/ethnicity, age at menarche, age at first birth, duration of lactation, family history of breast cancer

** unstable model

Table 22. Relative frequencies of HLA **Class I A** allele distributions by allele and breast cancer case-control status by disease stage at diagnosis for cases, and all controls, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	Localized stage (cases)			HLA-A allele	Regional/Remote stage (cases)		
	Cases N=313	Controls N=493	p*		Cases N=107	Controls N=483	p*
1	14.4	19.3	0.08	**1**	26.2	19.3	0.11
2	47.3	44.9	0.51	**2**	44.9	44.9	1.00
3	20.5	16.8	0.19	**3**	17.8	16.8	0.81
11	8.3	9.3	0.63	**11**	**2.8**	**9.3**	**0.03**
23	**12.1**	**6.6**	**0.01**	**23**	4.7	6.6	0.45
24	14.1	17.2	0.24	**24**	14.0	17.2	0.43
25	1.3	2.3	0.31	**25**	1.9	2.3	1.00
26	4.8	5.6	0.63	**26**	5.6	5.6	0.99
29	9.0	6.8	0.27	**29**	9.4	6.8	0.37
30	9.3	11.6	0.30	**30**	**19.6**	**11.6**	**0.03**
31	6.4	5.8	0.73	**31**	8.4	5.8	0.31
32	5.4	5.6	0.92	**32**	3.7	5.6	0.44
33	**8.0**	**4.6**	**0.04**	**33**	5.6	4.6	0.64
34	3.8	2.9	0.47	**34**	2.8	2.9	1.00
36	1.0	1.0	1.00	**36**	0.9	1.0	1.00
66	3.2	2.7	0.68	**66**	0.9	2.7	0.48
68	15.7	17.0	0.62	**68**	15.0	17.0	0.61
69	0.0	0.2	1.00	**69**	0.0	0.2	1.00
74	3.2	5.0	0.23	**74**	3.7	5.0	0.59
80	0.3	0.4	1.00	**80**	0.0	0.4	1.00

* chi-square or Fisher's exact test

Table 23 Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class I A** alleles most strongly with breast cancer risk for localized and regional/remote stage cases vs all controls, post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	Localized stage (cases)			HLA-A allele	Regional/Remote stage (cases)		
	Pop. prev.*	**OR****	**95% CI**		***Pop. prev.****	**OR****	**95% CI**
1	***19.3***	**0.7**	**0.5 – 0.99**	**1**	*19.3*	1.3	0.8 – 2.2
2	*44.9*	1.1	0.8 – 1.4	**2**	*44.9*	1.1	0.7 – 1.7
3	*16.8*	1.3	0.9 – 1.8	**3**	*16.8*	1.2	0.7 – 2.1
11	*9.3*	0.9	0.5 – 1.4	**11**	***9.3***	**0.3**	**0.1 – 1.0**
23	***6.6***	**1.7**	**1.1 – 2.8**	**23**	*6.6*	0.7	0.3 – 1.8
24	*17.2*	0.8	0.5 – 1.2	**24**	*17.2*	0.7	0.4 – 1.3
25	*2.3*	0.5	0.2 – 1.7	**25**	*2.3*	0.8	0.2 – 3.9
26	*5.6*	0.8	0.4 – 1.6	**26**	*5.6*	1.0	0.4 – 2.6
29	*6.8*	1.3	0.8 – 2.1	**29**	*6.8*	1.7	0.8 – 3.5
30	*11.6*	0.8	0.5 – 1.2	**30**	***11.6***	**1.9**	**1.0 – 3.4**
31	*5.8*	1.2	0.7 – 2.2	**31**	*5.8*	1.2	0.5 – 2.9
32	*5.6*	1.0	0.6 – 1.8	**32**	*5.6*	0.8	0.3 – 2.4
33	***4.6***	**2.3**	**1.3 – 4.1**	**33**	*4.6*	1.3	0.5 – 3.3
34	*2.9*	0.9	0.4 – 2.0	**34**	*2.9*	0.9	0.2 – 3.3
36	*1.0*	1.3	0.3 – 5.1	**36**	*1.0*	0.5	0.04 – 5.9
66	*2.7*	1.2	0.5 – 2.7	**66**	*2.7*	0.3	0.04 – 2.4
68	*17.0*	1.0	0.7 – 1.5	**68**	*17.0*	0.9	0.5 – 1.6
69	*0.2*	***		**69**	*0.2*	***	
74	*5.0*	0.7	0.3 – 1.3	**74**	*5.0*	0.6	0.2 – 2.0
80	*0.4*	0.7	0.1 - 8.0	**80**	*0.4*	***	

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 24. Relative frequencies of statistically significant HLA **Class I A** allele distributions by allele and by **disease stage of cases** vs all controls, white post-menopausal women, Greater Bay Area, 1997-1999

WHITES							
HLA-A allele	Localized stage (cases)			HLA-A allele	Regional/Remote stage (cases)		
	Cases N=119	Controls N=159	p*		Cases N=33	Controls N=159	p*
1				1			
2				2			
3				3			
11				11			
23	**8.4**	**1.9**	**0.01**	23	6.1	1.9	0.20
24				24			
25				25			
26				26			
29				29			
30				30			
31				31			
32				32			
33				33			
34				34			
36				36			
66				66			
68				68			
69				69			
74				74			
80				80			

* chi-square or Fisher's exact test

Table 25. Relative frequencies of statistically significant HLA **Class I A** allele distributions by allele and by **disease stage of cases** vs all controls, black post-menopausal women, Greater Bay Area, 1997-1999

BLACKS							
HLA-A allele	**Localized stage (cases)**			**HLA-A allele**	**Regional/Remote stage (cases)**		
	Cases N=97	**Controls N=140**	**p**		**Cases N=34**	**Controls N=140**	**P**
1				**1**			
2				**2**			
3				**3**			
11				**11**			
23				**23**			
24				**24**			
25				**25**			
26				**26**			
29				**29**			
30				**30**			
31				**31**			
32	**7.2**	**0.7**	**0.01**	**32**	2.9	0.7	0.35
33	**15.5**	**7.1**	**0.04**	**33**	5.9	7.1	1.00
34				**34**			
36				**36**			
66				**66**			
68				**68**			
69				**69**			
74				**74**			
80				**80**			

* chi-square or Fisher's exact test

Table 26. Relative frequencies of statistically significant HLA **Class I A** allele distributions by allele and by **disease stage of cases** vs all controls, Hispanic post-menopausal women, Greater Bay Area, 1997-1999

HISPANICS							
HLA-A allele	**Localized stage (cases)**			**HLA-A allele**	**Regional/Remote stage (cases)**		
	Cases N=97	**Controls N=184**	**p***		**Cases N=40**	**Controls N=184**	**p***
1	**7.2**	**20.1**	**0.005**	**1**	22.5	20.1	0.73
2				**2**			
3				**3**			
11				**11**			
23				**23**			
24				**24**			
25				**25**			
26				**26**			
29				**29**			
30				**30**			
31				**31**			
32				**32**			
33				**33**			
34				**34**			
36				**36**			
66				**66**			
68				**68**			
69				**69**			
74				**74**			
80				**80**			

* chi-square or Fisher's exact test

Table 27. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class I A** alleles most strongly with breast cancer risk for **localized stage** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
A-01		1.0	0.6 – 1.8		0.7	0.3 – 1.7	***20.1***	**0.3**	**0.1 – 0.7**
A-11		0.8	0.4 – 1.7		1.9	0.4 – 8.0		0.8	0.3 – 1.9
A-23	***1.9***	**4.2**	**1.1 – 16.5**		1.4	0.7 – 2.7		2.3	0.7 – 7.2
A-32		0.6	0.2 – 1.5	***0.7***	**12.1**	**1.4–102.5**		0.4	0.1 – 1.6
A-33		1.7	0.4 – 6.8	***7.1***	**3.0**	**1.3 – 7.3**		1.6	0.4 – 5.4

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer

Table 28. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class I A** alleles most strongly with breast cancer risk for **regional/remote stage** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. Prev****	**OR****	**95% CI**
A-01		1.8	0.8 – 4.0		1.7	0.6 – 5.2		1.1	0.5 – 2.6
A-11		0.2	0.02 – 1.3		***			0.6	0.1 – 2.9
A-23		2.9	0.4 – 19.3		0.6	0.1 – 2.0		***	
A-32		1.1	0.3 – 4.2		6.4	0.3–126.8		***	
A-33		1.0	0.1 – 10.0		1.0	0.2 – 5.1		1.9	0.4 – 7.9

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 29. Relative frequencies of HLA **Class I A** allele distributions by allele and breast cancer case-control status by ER status of tumors for cases, and all controls, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	ER-Positive (cases)			HLA-A allele	ER-Negative (cases)		
	Cases N=280	Controls N=483	p*		Cases N=75	Controls N=483	p*
1	18.6	19.3	0.82	**1**	**9.3**	**19.3**	**0.04**
2	48.6	44.9	0.33	**2**	38.7	44.9	0.31
3	20.7	16.8	0.17	**3**	21.3	16.8	0.33
11	**4.6**	**9.3**	**0.02**	**11**	9.3	9.3	1.00
23	9.6	6.6	0.13	**23**	10.7	6.6	0.21
24	13.9	17.2	0.23	**24**	10.7	17.2	0.16
25	1.4	2.3	0.42	**25**	1.3	2.3	1.00
26	6.8	5.6	0.50	**26**	1.3	5.6	0.16
29	9.6	6.8	0.16	**29**	8.0	6.8	0.71
30	11.1	11.6	0.83	**30**	16.0	11.6	0.28
31	7.9	5.8	0.27	**31**	8.0	5.8	0.44
32	6.4	5.6	0.64	**32**	2.7	5.6	0.41
33	6.8	4.6	0.19	**33**	**13.3**	**4.6**	**0.01**
34	2.9	2.9	0.97	**34**	1.3	2.9	0.71
36	0.7	1.0	1.00	**36**	2.7	1.0	0.24
66	1.8	2.7	0.43	**66**	5.3	2.7	0.27
68	13.6	17.0	0.21	**68**	22.7	17.0	0.23
69	0.0	0.2	1.00	**69**	0.0	0.2	1.00
74	3.2	5.0	0.25	**74**	4.0	5.0	1.00
80	0.4	0.4	1.00	**80**	0.0	0.4	1.00

* chi-square or Fisher's exact test

Table 30. Adjusted* odds ratios and 95% confidence intervals for associations of HLA **class I A** alleles with breast cancer risk for ER-positive and ER-negative cases vs all controls, post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	ER-positive (cases)			HLA-A allele	ER-negative (cases)		
	Pop. prev.*	**OR****	**95% CI**		***Pop. prev.****	**OR****	**95% CI**
1	*19.3*	0.9	0.6 – 1.3	**1**	*19.3*	0.5	0.2 – 1.1
2	*44.9*	1.2	0.9 – 1.6	**2**	*44.9*	0.9	0.5 – 1.5
3	*16.8*	1.3	0.8 – 1.8	**3**	*16.8*	1.4	0.7 – 2.7
11	***9.3***	**0.4**	**0.2 – 0.8**	**11**	*9.3*	1.5	0.6 – 3.6
23	*6.6*	1.6	0.9 – 2.8	**23**	*6.6*	1.1	0.4 – 2.6
24	*17.2*	0.8	0.5 – 1.2	**24**	*17.2*	0.7	0.3 – 1.5
25	*2.3*	0.6	0.2 – 1.9	**25**	*2.3*	0.6	0.1 – 5.1
26	*5.6*	1.2	0.7 – 2.3	**26**	*5.6*	0.2	0.03 – 1.7
29	*6.8*	1.4	0.8 – 2.5	**29**	*6.8*	1.5	0.6 – 3.8
30	*11.6*	1.0	0.6 – 1.6	**30**	*11.6*	1.0	0.5 – 2.1
31	*5.8*	1.4	0.8 – 2.6	**31**	*5.8*	1.3	0.5 – 3.8
32	*5.6*	1.1	0.6 – 2.1	**32**	*5.6*	0.6	0.1 – 2.8
33	*4.6*	1.8	0.9 – 3.5	**33**	***4.6***	**2.8**	**1.2 – 6.6**
34	*2.9*	1.1	0.4 – 2.9	**34**	*2.9*	0.3	0.03 – 2.2
36	*1.0*	0.8	0.1 – 4.1	**36**	*1.0*	1.9	0.3 – 10.5
66	*2.7*	0.6	0.2 – 1.8	**66**	*2.7*	1.4	0.4 – 4.7
68	*17.0*	0.8	0.5 – 1.3	**68**	*17.0*	1.4	0.8 – 2.6
69	*0.2*	***		**69**	*0.2*	***	
74	*5.0*	0.7	0.3 – 1.5	**74**	*5.0*	0.6	0.2 – 2.0
80	*0.4*	1.1	0.1 – 12.6	**80**	*0.4*	***	

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 31. Relative frequencies of statistically significant HLA **Class I A** allele distributions by allele and **ER status of tumors** in cases vs all controls, white post-menopausal women, Greater Bay Area, 1997-1999

WHITES							
HLA-A allele	ER-Positive (cases)			HLA-A allele	ER-Negative (cases)		
	Cases N=117	Controls N=159	P		Cases N=14	Controls N=159	P
1				1			
2				2			
3				3			
11	**6.8**	**15.1**	**0.03**	11	21.4	15.1	0.46
23	**8.6**	**1.9**	**0.01**	23	0.0	1.9	1.00
24	**7.7**	**17.0**	**0.02**	24	14.3	17.0	1.00
25				25			
26				26			
29				29			
30				30			
31				31			
32				32			
33				33			
34				34			
36				36			
66				66			
68				68			
69				69			
74				74			
80				80			

Table 32. Relative frequencies of statistically significant HLA **Class I A** allele distributions by allele and **ER status of tumors** in cases vs all controls, black post-menopausal women, Greater Bay Area, 1997-1999

BLACKS							
HLA-A allele	**ER-Positive (cases)**			**HLA-A allele**	**ER-Negative (cases)**		
	Cases N=69	**Controls N=140**	**P**		**Cases N=37**	**Controls N=140**	**P**
1	7.3	11.4	0.34	**1**	5.4	11.4	0.37
2				**2**			
3				**3**			
11				**11**			
23				**23**			
24				**24**			
25				**25**			
26				**26**			
29				**29**			
30				**30**			
31				**31**			
32	**7.3**	**0.7**	**0.02**	**32**	5.4	0.7	0.11
33	8.7	7.1	0.69	**33**	**24.3**	**7.1**	**0.01**
34				**34**			
36				**36**			
66				**66**			
68				**68**			
69				**69**			
74				**74**			
80				**80**			

Table 33. Relative frequencies of statistically significant HLA **Class I A** allele distributions by allele and **ER status of tumors** in cases vs all controls, Hispanic post-menopausal women, Greater Bay Area, 1997-1999

HISPANICS							
HLA-A allele	ER-Positive (cases)			HLA-A allele	ER-Negative (cases)		
	Cases N=94	Controls N=184	P		Cases N=24	Controls N=184	P
1				1			
2				2			
3				3			
11				11			
23				23			
24				24			
25				25			
26				26			
29				29			
30				30			
31				31			
32				32			
33				33			
34				34			
36				36			
66				66			
68				68			
69				69			
74				74			
80				80			

Table 34. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class I A** alleles most strongly with breast cancer risk for **ER positive cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
A-01		1.2	0.7 – 2.1		0.6	0.2 – 1.8		0.6	0.3 – 1.2
A-11	***15.1***	**0.4**	**0.2 – 0.9**		0.7	0.1 – 7.0		0.4	0.1 – 1.4
A-23	***1.9***	**4.3**	**1.1 – 16.9**		0.9	0.4 – 2.0		2.2	0.7 – 7.1
A-24	***17.0***	**0.4**	**0.2 – 0.9**		0.8	0.2 – 2.6		1.1	0.6 – 2.0
A-32		0.9	0.3 – 2.1	***0.7***	**12.6**	**1.4–115.2**		0.4	0.1 – 1.6
A-33		2.1	0.6 – 7.8		1.4	0.5 – 4.2		2.4	0.8 – 7.4

Table 35. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class I A** alleles most strongly with breast cancer risk for **ER negative cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-A allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. Prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
A-01		***			0.5	0.1 – 2.3		0.4	0.1 – 1.8
A-11		***			3.0	0.5 – 18.8		1.0	0.2 – 5.1
A-23		***			1.3	0.5 – 3.4		1.0	0.1 – 9.3
A-24		***			0.4	0.04 - 3.0		0.8	0.3 – 2.3
A-32		***		*0.7*	9.3	0.7-117.9		***	
A-33		***		***7.1***	**5.9**	**2.0 – 17.2**		1.1	0.1 – 9.4

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 36. Relative frequencies of HLA **Class I B** allele distributions by allele and breast cancer case-control status by **disease stage at diagnosis** for cases, and all controls, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	Localized stage (cases)			HLA-B allele	Regional/Remote stage (cases)		
	Cases N=314	Controls N=484	p*		Cases N=107	Controls N=484	p*
7	18.5	15.9	0.35	**7**	18.7	15.9	0.48
8	10.8	11.2	0.88	**8**	14.0	11.2	0.40
13	**2.2**	**5.2**	**0.04**	**13**	2.8	5.2	0.30
14	7.0	7.0	0.99	**14**	7.5	7.0	0.87
15	18.8	13.8	0.06	**15**	14.0	13.8	0.96
18	7.3	7.0	0.87	**18**	8.4	7.0	0.62
27	5.1	6.6	0.38	**27**	1.9	6.6	0.06
35	17.2	19.2	0.47	**35**	23.4	19.2	0.33
37	0.6	1.9	0.22	**37**	2.8	1.9	0.46
38	2.2	3.5	0.30	**38**	2.8	3.5	1.00
39	**4.8**	**8.5**	**0.05**	**39**	5.6	8.5	0.32
40	14.0	12.2	0.45	**40**	15.0	12.2	0.44
41	2.6	1.2	0.17	**41**	0.9	1.2	1.00
42	3.5	4.8	0.39	**42**	2.8	4.8	0.60
44	22.6	18.6	0.17	**44**	24.3	18.6	0.18
45	3.5	5.0	0.33	**45**	1.9	5.0	0.20
47	0.32	1.0	0.41	**47**	1.9	1.0	0.62
48	1.9	1.9	0.96	**48**	1.9	1.9	1.00
49	4.5	4.3	0.94	**49**	6.5	4.3	0.33
50	1.6	3.7	0.08	**50**	1.9	3.7	0.55
51	11.5	8.3	0.13	**51**	6.5	8.3	0.55
52	3.2	3.5	0.80	**52**	5.6	3.5	0.28
53	7.6	9.7	0.32	**53**	10.3	9.7	0.86
54	0.3	0.0	0.39	**54**	0.0	0.0	0.00
55	2.9	1.9	0.35	**55**	1.9	1.9	1.00
56	0.3	1.2	0.26	**56**	0.0	1.2	0.60
57	4.1	6.6	0.14	**57**	5.9	6.6	0.70
58	7.0	4.8	0.18	**58**	6.5	4.8	0.45
73	0.3	0.0	0.39	**73**	--	--	
78	1.6	0.8	0.33	**78**	0.9	0.8	1.00
81	1.0	0.8	1.00	**81**	0.9	0.8	1.00
82	0.3	0.6	1.00	**82**	0.0	0.6	1.00

* chi-square or Fisher's exact test

Table 37. Adjusted* odds ratios and 95% confidence intervals for associations of HLA **class I B** alleles with breast cancer risk for localized and regional/remote stage cases vs all controls, post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	Localized stage (cases)			HLA-B allele	Regional/Remote stage (cases)		
	Pop. prev.*	OR**	95% CI		***Pop. prev.****	OR**	95% CI
7	*15.9*	1.1	0.8-1.6	**7**	*15.9*	1.3	0.7-2.3
8	*11.2*	0.9	0.6-1.5	**8**	*11.2*	1.3	0.7-2.5
13	***5.2***	**0.4**	**0.2-1.0**	**13**	*5.2*	0.6	0.2-2.1
14	*7.0*	1.1	0.6-1.8	**14**	*7.0*	1.1	0.5-2.6
15	***13.8***	**1.5**	**1.0-2.2**	**15**	*13.8*	1.0	0.5-1.8
18	*7.0*	1.0	0.6-1.7	**18**	*7.0*	1.1	0.5-2.4
27	*6.6*	0.8	0.4-1.4	**27**	*6.6*	0.3	0.1-1.2
35	*19.2*	0.8	0.6-1.2	**35**	*19.2*	1.4	0.9-2.4
37	*1.9*	0.3	0.1-1.5	**37**	*1.9*	1.7	0.4-6.6
38	*3.5*	0.7	0.3-1.6	**38**	*3.5*	0.8	0.2-3.0
39	*8.5*	0.6	0.3-1.2	**39**	*8.5*	0.5	0.2-1.2
40	*12.2*	1.3	0.9-2.0	**40**	*12.2*	1.4	0.8-2.6
41	***1.2***	**3.8**	**1.4-10.1**	**41**	*1.2*	0.8	0.1-6.9
42	*4.8*	0.7	0.4-1.6	**42**	*4.8*	0.5	0.1-1.7
44	*18.6*	1.1	0.8-1.6	**44**	***18.6***	**1.6**	**1.0-2.7**
45	*5.0*	0.7	0.3-1.4	**45**	*5.0*	0.3	0.1-1.5
47	*1.0*	***		**47**	*1.0*	2.1	0.4-10.9
48	*1.9*	1.5	0.5-4.1	**48**	*1.9*	1.0	0.2-4.8
49	*4.3*	1.2	0.6-2.3	**49**	*4.3*	1.2	0.5-3.1
50	*3.7*	0.4	0.1-1.1	**50**	*3.7*	0.5	0.1-2.1
51	*8.3*	1.4	0.9-2.2	**51**	*8.3*	0.9	0.4-2.0
52	*3.5*	1.0	0.5-2.2	**52**	*3.5*	1.6	0.6-4.3
53	*9.7*	0.8	0.5-1.3	**53**	*9.7*	1.0	0.5-2.1
54	*0.0*	4.6	0.1-182.4	**54**	--	--	--
55	*1.9*	1.1	0.4-2.8	**55**	*1.9*	0.9	0.2-4.5
56	*1.2*	0.3	0.0-2.2	**56**	*1.2*	***	
57	*6.6*	0.6	0.3-1.2	**57**	*6.6*	0.9	0.4-2.3
58	*4.8*	1.4	0.8-2.6	**58**	*4.8*	0.9	0.3-2.5
73	--	2.3	0.1-90.7	**73**	--	--	--
78	*0.8*	1.7	0.5-5.8	**78**	*0.8*	1.0	0.1-8.9
81	*0.8*	0.9	0.2-4.1	**81**	*0.8*	1.0	0.1-9.6
82	*0.6*	0.5	0.0-4.4	**82**	*0.6*	***	

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 38. Relative frequencies of statistically significant HLA **Class I B** allele distributions by allele and by **disease stage of cases** vs all controls, white post-menopausal women, Greater Bay Area, 1997-1999

WHITES							
HLA-B allele	Localized stage (cases)		p*	HLA-B allele	Regional/Remote stage (cases)		p*
	Cases N=119	Controls N=160			Cases N=33	Controls N=160	
7				7			
8				8			
13				13			
14				14			
15				15			
18				18			
27				27			
35				35			
37				37			
38				38			
39				39			
40				40			
41				41			
42				42			
44				44			
45				45			
47				47			
48				48			
49				49			
50				50			
51				51			
52				52			
53				53			
54				54			
55				55			
56				56			
57				57			
58	0.0	1.3	0.51	**58**	**9.1**	**1.3**	**0.04**
73				73			
78				78			
81				81			
82				82			

* chi-square or Fisher's exact test

Table 39. Relative frequencies of statistically significant HLA **Class I B** allele distributions by allele and by **disease stage of cases** vs all controls, black post-menopausal women, Greater Bay Area, 1997-1999

BLACKS							
HLA-B allele	Localized stage (cases)			HLA-B allele	Regional/Remote stage (cases)		
	Cases N=97	Controls N=140	p*		Cases N=34	Controls N=140	p*
7				7			
8				8			
13				13			
14				14			
15				15			
18				18			
27				27			
35				35			
37				37			
38				38			
39				39			
40				40			
41				41			
42				42			
44				44			
45				45			
47				47			
48				48			
49				49			
50				50			
51				51			
52				52			
53				53			
54				54			
55				55			
56				56			
57				57			
58				58			
73				73			
78				78			
81				81			
82				82			

* chi-square or Fisher’s exact test

Table 40. Relative frequencies of statistically significant HLA **Class I B** allele distributions by allele and by **disease stage of cases** vs all controls, Hispanic post-menopausal women, Greater Bay Area, 1997-1999

HISPANICS							
HLA-B allele	**Localized stage (cases)**			**HLA-B allele**	**Regional/Remote stage (cases)**		
	Cases N=98	**Controls N=183**	**p***		**Cases N=40**	**Controls N=184**	**p***
7				**7**			
8				**8**			
13				**13**			
14				**14**			
15	14.3	9.2	0.20	**15**	20.0	9.2	0.09
18				**18**			
27				**27**			
35	27.6	23.9	0.50	**35**	**42.5**	**23.9**	**0.02**
37				**37**			
38				**38**			
39				**39**			
40	**27.6**	**17.4**	**0.05**	**40**	20.0	17.4	0.70
41				**41**			
42				**42**			
44				**44**			
45				**45**			
47				**47**			
48				**48**			
49				**49**			
50				**50**			
51				**51**			
52				**52**			
53				**53**			
54				**54**			
55				**55**			
56				**56**			
57				**57**			
58				**58**			
73				**73**			
78				**78**			
81				**81**			
82				**82**			

* chi-square or Fisher's exact test

Table 41. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class I B** alleles most strongly with breast cancer risk for **localized stage cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. Prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
B-15		1.7	0.8 – 3.4		1.2	0.6 – 2.2		1.7	0.8 – 3.8
B-35		0.8	0.4 – 1.5		0.8	0.3 – 1.9		1.3	0.7 – 2.3
B-40		1.1	0.5 – 2.2		0.6	0.1 – 2.9	***17.4***	**1.9**	**1.03 – 3.6**
B-58		***			1.5	0.7 – 3.2		2.8	0.6 – 13.4

Table 42. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class I B** alleles most strongly with breast cancer risk for **regional/remote stage** cases vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. Prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
B-15		0.5	0.1 – 2.6		0.5	0.2 – 1.6		2.2	0.8 – 5.8
B-35		0.9	0.3 – 2.7		0.7	0.2 – 2.7	***23.9***	**2.2**	**1.1 – 4.6**
B-40		1.4	0.5 – 4.3		2.2	0.5 – 10.0		1.5	0.6 – 3.8
B-58		5.2	0.6 – 42.7		0.6	0.2 – 2.3		1.5	0.1 – 16.0

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 43**.** Relative frequencies of HLA **Class I B** allele distributions by allele and breast cancer case-control status by **ER status of tumors** for cases, and all controls, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	ER-Positive (cases)			HLA-B allele	ER-Negative (cases)		
	Cases N=281	Controls N=484	p*		Cases N=75	Controls N=484	p*
7	18.9	15.9	0.29	**7**	18.7	15.9	0.55
8	13.9	11.2	0.27	**8**	5.3	11.2	0.12
13	2.9	5.2	0.13	**13**	1.3	5.2	0.23
14	8.2	7.0	0.56	**14**	5.3	7.0	0.59
15	15.0	13.8	0.67	**15**	**24.0**	**13.8**	**0.02**
18	8.2	7.0	0.56	**18**	4.0	7.0	0.46
27	5.3	6.6	0.48	**27**	2.7	6.6	0.30
35	18.9	19.2	0.90	**35**	18.7	19.2	0.91
37	1.4	1.9	0.78	**37**	1.33	1.9	1.00
38	3.6	3.5	0.97	**38**	0.0	3.5	0.10
39	5.3	8.5	0.11	**39**	5.3	8.5	0.35
40	15.3	12.2	0.22	**40**	13.3	12.2	0.78
41	1.8	1.2	0.54	**41**	**5.3**	**1.2**	**0.03**
42	**1.8**	**4.8**	**0.03**	**42**	5.3	4.8	0.77
44	23.1	18.6	0.13	**44**	16.0	18.6	0.59
45	2.5	5.0	0.10	**45**	4.0	5.0	1.00
47	0.7	1.0	1.00	**47**	1.3	1.0	0.58
48	2.5	1.9	0.56	**48**	1.3	1.9	1.00
49	5.0	4.3	0.68	**49**	6.7	4.3	0.37
50	1.8	3.7	0.13	**50**	1.3	3.7	0.49
51	11.0	8.3	0.20	**51**	8.0	8.3	0.94
52	2.1	3.5	0.28	**52**	6.7	3.5	0.20
53	7.5	9.7	0.29	**53**	13.3	9.7	0.33
54	0.4	0.0	0.37	**54**	--	--	
55	2.9	1.9	0.37	**55**	0.0	1.9	0.62
56	0.4	1.2	0.43	**56**	0.0	1.2	1.00
57	3.9	6.6	0.12	**57**	9.3	6.6	0.39
58	4.3	4.8	0.76	**58**	9.3	4.8	0.10
73	--	--		**73**	--	--	
78	1.8	0.8	0.30	**78**	1.3	0.8	0.51
81	1.1	0.8	0.71	**81**	0.0	0.8	1.00
82	0.4	0.6	1.00	**82**	0.0	0.6	1.00

* chi-square or Fisher's exact test

Table 44. Adjusted* odds ratios and 95% confidence intervals for associations of HLA **class I B** alleles with breast cancer risk for ER-positive and ER-negative cases vs all controls, post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	ER-positive (cases)			HLA-B allele	ER-negative (cases)		
	Pop. prev.*	**OR****	**95% CI**		***Pop. prev.****	**OR****	**95% CI**
7	*15.9*	1.2	0.8-1.8	**7**	*15.9*	1.2	0.6-2.5
8	*11.2*	1.1	0.7-1.8	**8**	*11.2*	0.6	0.2-1.9
13	*5.2*	0.5	0.2-1.2	**13**	*5.2*	0.3	0.0-2.5
14	*7.0*	1.2	0.7-2.0	**14**	*7.0*	0.9	0.3-2.8
15	*13.8*	1.2	0.8-1.8	**15**	*13.8*	1.6	0.8-2.9
18	*7.0*	1.3	0.7-2.3	**18**	*7.0*	0.5	0.1-1.6
27	*6.6*	0.7	0.4-1.4	**27**	*6.6*	0.4	0.1-2.0
35	*19.2*	1.0	0.7-1.5	**35**	*19.2*	1.1	0.6-2.2
37	*1.9*	0.7	0.2-2.4	**37**	*1.9*	1.1	0.1-9.5
38	*3.5*	1.0	0.4-2.3	**38**	*3.5*	***	
39	*8.5*	0.6	0.3-1.2	**39**	*8.5*	0.6	0.2-1.8
40	*12.2*	1.3	0.8-2.0	**40**	*12.2*	1.6	0.7-3.4
41	*1.2*	1.6	0.5-5.5	**41**	***1.2***	**4.5**	**1.2-17.8**
42	*4.8*	0.4	0.2-1.2	**42**	*4.8*	0.7	0.2-2.1
44	*18.6*	1.2	0.8-1.7	**44**	*18.6*	1.1	0.5-2.2
45	*5.0*	0.6	0.2-1.3	**45**	*5.0*	0.6	0.2-2.0
47	*1.0*	0.3	0.0-3.0	**47**	*1.0*	1.5	0.2-13.7
48	*1.9*	1.7	0.6-4.7	**48**	*1.9*	0.9	0.1-7.9
49	*4.3*	1.3	0.6-2.6	**49**	*4.3*	1.0	0.3-3.2
50	*3.7*	0.5	0.2-1.4	**50**	*3.7*	0.3	0.0-2.6
51	*8.3*	1.3	0.8-2.2	**51**	*8.3*	1.3	0.5-3.2
52	*3.5*	0.6	0.2-1.6	**52**	*3.5*	1.9	0.6-5.5
53	*9.7*	0.8	0.5-1.5	**53**	*9.7*	1.0	0.5-2.2
54	*0.0*	***		**54**	*0.0*	--	--
55	*1.9*	1.3	0.5-3.5	**55**	*1.9*	***	
56	*1.2*	0.3	0.0-2.2	**56**	*1.2*	***	
57	*6.6*	0.6	0.3-1.1	**57**	*6.6*	1.3	0.5-3.3
58	*4.8*	1.0	0.5-2.1	**58**	*4.8*	1.2	0.4-3.1
73	--	--	--	**73**	--	--	--
78	*0.8*	2.3	0.6-8.7	**78**	*0.8*	1.0	0.1-9.9
81	*0.8*	1.7	0.4-8.1	**81**	*0.8*	***	
82	*0.6*	0.6	0.1-6.3	**82**	*0.6*	***	

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 45. Relative frequencies of statistically significant HLA **Class I B** allele distributions by allele and **ER status of tumors** in cases vs all controls, white post-menopausal women, Greater Bay Area, 1997-1999

WHITES							
HLA-B allele	ER-positive (cases)			HLA-B allele	ER-negative (cases)		
	Cases N=117	Controls N=160	p*		Cases N=14	Controls N=160	p*
7	23.1	20.0	0.54	**7**	**50.0**	**20.0**	**0.02**
8				8			
13				13			
14				14			
15				15			
18				18			
27				27			
35				35			
37				37			
38				38			
39				39			
40				40			
41				41			
42				42			
44				44			
45				45			
47				47			
48				48			
49				49			
50				50			
51				51			
52				52			
53				53			
54				54			
55				55			
56				56			
57				57			
58				58			
73				73			
78				78			
81				81			
82				82			

***** chi-square or Fisher's exact test

Table 46. Relative frequencies of statistically significant HLA **Class I B** allele distributions by allele and **ER status of tumors** in cases vs all controls, black post-menopausal women, Greater Bay Area, 1997-1999

BLACKS							
HLA-B allele	ER-positive (cases)			HLA-B allele	ER-negative (cases)		
	Cases N=69	Controls N=140	p*		Cases N=37	Controls N=140	p*
7	**24.6**	**12.1**	**0.02**	**7**	13.5	12.1	0.78
8				**8**			
13				**13**			
14				**14**			
15				**15**			
18				**18**			
27				**27**			
35				**35**			
37				**37**			
38				**38**			
39				**39**			
40				**40**			
41				**41**			
42	**4.4**	**14.3**	**0.03**	**42**	10.8	14.3	0.58
44				**44**			
45				**45**			
47				**47**			
48				**48**			
49				**49**			
50				**50**			
51				**51**			
52				**52**			
53				**53**			
54				**54**			
55				**55**			
56				**56**			
57				**57**			
58				**58**			
73				**73**			
78				**78**			
81				**81**			
82				**82**			

* chi-square or Fisher's exact test

Table 47. Relative frequencies of statistically significant HLA **Class I B** allele distributions by allele and **ER status of tumors** in cases vs all controls, Hispanic post-menopausal women, Greater Bay Area, 1997-1999

HISPANICS							
HLA-B allele	ER-positive (cases)			HLA-B allele	ER-negative (cases) (cases)		
	Cases N=95	Controls N=184	p*		Cases N=24	Controls N=184	p*
7				7			
8				8			
13				13			
14				14			
15				15			
18				18			
27				27			
35				35			
37				37			
38				38			
39				39			
40				40			
41	2.1	1.1	0.61	41	8.3	1.1	0.07
42				42			
44				44			
45				45			
47				47			
48				48			
49				49			
50				50			
51				51			
52	3.2	3.8	1.0	52	**16.7**	**3.8**	**0.03**
53				53			
54				54			
55				55			
56				56			
57				57			
58				58			
73				73			
78				78			
81				81			
82				82			

* chi-square or Fisher's exact test

Table 48. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class I B** alleles most strongly with breast cancer risk for **ER positive cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
B-07		1.2	0.6 – 2.1	***12.1***	**2.3**	**1.1 – 5.0**		0.5	0.2 – 1.2
B-41		3.9	0.4 – 38.4		***			2.4	0.3 – 18.3
B-42		1.7	0.9 – 3.1		0.3	0.1 – 1.1		1.5	0.2 – 9.5
B-52		0.8	0.2 – 3.6		***			0.9	0.2 – 3.5

Table 49. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class I B** alleles most strongly with breast cancer risk for **ER negative cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-B allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. Prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
B-07		***			1.1	0.4 – 3.5		0.5	0.1 – 2.1
B-41		***			3.0	0.4 – 21.2	***1.1***	**13.5**	**1.6 – 111.5**
B-42		***			0.7	0.2 – 2.3		***	
B-52		***			0.6	0.1 – 5.6	***3.8***	**5.6**	**1.4 – 22.9**

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 50. Relative frequencies of HLA **Class II DRB1** allele distributions by allele and breast cancer case-control status **by disease stage at diagnosis** for cases, and all controls, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-DRB1 allele	Localized stage (cases)			HLA-DRB1 allele	Regional/Remote stage (cases)		
	Cases N=310	Controls N=479	p*		Cases N=107	Controls N=479	p*
1	17.1	16.7	0.88	**1**	16.8	16.7	0.98
3	18.1	18.6	0.86	**3**	21.5	18.6	0.49
4	26.5	30.3	0.25	**4**	27.1	30.3	0.52
7	22.3	19.2	0.70	**7**	21.5	19.2	0.59
8	15.2	12.5	0.29	**8**	12.2	12.5	0.92
9	2.6	2.5	0.95	**9**	0.9	2.5	0.48
10	1.3	2.1	0.41	**10**	0.93	2.1	0.70
11	19.4	17.8	0.57	**11**	15.9	17.8	0.65
12	4.8	4.4	0.77	**12**	2.8	4.4	0.60
13	24.8	25.3	0.89	**13**	29.0	25.3	0.43
14	9.4	10.9	0.50	**14**	12.2	10.9	0.70
15	22.6	24.0	0.64	**15**	21.5	24.0	0.58
16	2.9	3.1	0.86	**16**	4.7	3.1	0.39

* chi-square or Fisher's exact test

Table 51. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DRB1** alleles most strongly with breast cancer risk for localized-stage and regional/remote-stage cases vs all controls, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DRB allele	Localized stage (cases)			HLA-DRB allele	Regional/remote (cases)		
	Pop. prev.*	**OR****	**95% CI**		***Pop. prev.****	**OR****	**95% CI**
1	*16.7*	1.0	0.7-1.5	**1**	*16.7*	1.0	0.6-1.9
3	*18.6*	1.0	0.7-1.4	**3**	*18.6*	1.2	0.7-2.0
4	*30.3*	0.9	0.6-1.2	**4**	*30.3*	0.9	0.6-1.5
7	*19.2*	1.0	0.7-1.5	**7**	*19.2*	1.2	0.7-2.1
8	*12.5*	1.3	0.9-2.0	**8**	*12.5*	1.0	0.5-1.9
9	*2.5*	1.4	0.6-3.3	**9**	*2.5*	0.3	0.0-2.2
10	*2.1*	0.8	0.2-2.4	**10**	*2.1*	0.4	0.0-3.0
11	*17.8*	1.1	0.8-1.6	**11**	*17.8*	0.8	0.5-1.5
12	*4.4*	1.2	0.6-2.3	**12**	*4.4*	0.5	0.2-1.8
13	*25.3*	1.0	0.7-1.4	**13**	*25.3*	1.1	0.7-1.8
14	*10.9*	0.9	0.5-1.4	**14**	*10.9*	1.0	0.5-2.0
15	*24.0*	0.9	0.6-1.2	**15**	*24.0*	0.9	0.6-1.6
16	*3.1*	1.0	0.4-2.2	**16**	*3.1*	1.5	0.5-4.5

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 52. Relative frequencies of statistically significant HLA **Class II DRB1** allele distributions by allele and by **disease stage of cases** vs all controls, white post-menopausal women, Greater Bay Area, 1997-1999

WHITES							
HLA-DRB allele	Localized stage (cases)			HLA-DRB allele	Regional/Remote stage (cases)		
	Cases N=116	Controls N=156	p*		Cases N=33	Controls N=156	p*
1				1			
3				3			
4				4			
7				7			
8				8			
9				9			
10				10			
11				11			
12				12			
13				13			
14				14			
15				15			
16				16			

* chi-square or Fisher's exact test

Table 53. Relative frequencies of statistically significant HLA **Class II DRB1** allele distributions by allele and by **disease stage of cases** vs all controls, black post-menopausal women, Greater Bay Area, 1997-1999

BLACKS							
HLA-DRB allele	Localized stage (cases)			HLA-DRB allele	Regional/Remote stage (cases)		
	Cases N=97	Controls N=140	p*		Cases N=34	Controls N=140	p*
1				1			
3	13.4	25.0	0.03	3	26.5	25.0	0.86
4				4			
7				7			
8				8			
9				9			
10				10			
11				11			
12				12			
13				13			
14				14			
15				15			
16	4.1	0.0	0.03	16	--	--	

* chi-square or Fisher's exact test

Table 54. Relative frequencies of statistically significant HLA **Class II DRB1** allele distributions by allele and by **disease stage of cases** vs all controls, Hispanic post-menopausal women, Greater Bay Area, 1997-1999

HISPANICS							
HLA-DRB allele	Localized stage (cases)			HLA-DRB allele	Regional/Remote stage (cases)		
	Cases N=97	Controls N=183	p*		Cases N=40	Controls N=183	p*
1				1			
3				3			
4				4			
7				7			
8	26.8	15.3	0.02	8	10.0	15.3	0.39
9				9			
10				10			
11				11			
12				12			
13				13			
14				14			
15				15			
16				16			

* chi-square or Fisher's exact test

Table 55. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DRB1** alleles most strongly with breast cancer risk for **localized stage** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DRB1 allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. Prev.****	**OR****	**95% CI**	***Pop. Prev****	**OR****	**95% CI**
DRB-3		1.1	0.6 – 2.0	***25.0***	**0.5**	**0.2 – 1.0**		1.7	0.8 – 3.3
DRB-8		0.8	0.3 – 2.0		1.2	0.5 – 2.6	***15.3***	**2.3**	**1.2 – 4.4**
DRB-16		0.6	0.1 – 2.6		***			0.4	0.1 – 2.0

Table 56. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DRB1** alleles most strongly with breast cancer risk for **regional/remote stage** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DRB1 allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. Prev****	**OR****	**95% CI**
DRB-3		1.4	0.5 – 3.6		1.2	0.5 – 2.9		1.4	0.5 – 3.9
DRB-8		0.3	0.04 – 2.5		2.2	0.8 – 5.9		0.6	0.2 – 1.9
DRB-16		2.7	0.6 – 12.3		0.4	0.1 – 1.8		1.0	0.2 – 5.0

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 57. Relative frequencies of HLA **Class II DRB1** allele distributions by allele and breast cancer case-control status **by ER status of tumor** for cases, and all controls, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-DRB allele	ER-Positive (cases)			HLA-DRB allele	ER-Negative (cases)		
	Cases N=277	Controls N=479	p*		Cases N=75	Controls N=479	p*
1	14.8	16.7	0.49	**1**	17.3	16.7	0.89
3	18.8	18.6	0.95	**3**	17.3	18.6	0.80
4	26.7	30.3	0.30	**4**	29.3	30.3	0.87
7	22.7	19.2	0.25	**7**	13.3	19.2	0.22
8	14.4	12.5	0.45	**8**	14.7	12.5	0.61
9	1.4	2.5	0.33	**9**	6.7	2.5	0.07
10	1.4	2.1	0.53	**10**	1.3	2.1	1.00
11	18.4	17.8	0.82	**11**	20.0	17.8	0.64
12	3.6	4.4	0.61	**12**	6.7	4.4	0.38
13	26.0	25.3	0.82	**13**	30.7	25.3	0.32
14	10.1	10.9	0.75	**14**	8.0	10.9	0.45
15	23.1	24.0	0.78	**15**	25.3	24.0	0.80
16	4.0	3.1	0.54	**16**	1.3	3.1	0.71

* chi-square or Fisher’s exact test

Table 58. Adjusted* odds ratios and 95% confidence intervals for associations of HLA **class II DRB1** alleles with breast cancer risk for ER-positive and ER-negative cases vs all controls, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DRB allele	ER-positive (cases)			HLA-DRB allele	ER-negative (cases)		
	Pop. prev.*	**OR****	**95% CI**		***Pop. prev.****	**OR****	**95% CI**
1	*16.7*	0.9	0.6-1.3	**1**	*16.7*	1.0	0.5-2.1
3	*18.6*	1.0	0.7-1.5	**3**	*18.6*	0.9	0.5-1.8
4	*30.3*	0.8	0.5-1.1	**4**	*30.3*	1.5	0.8-2.8
7	*19.2*	1.2	0.8-1.7	**7**	*19.2*	0.8	0.4-1.6
8	*12.5*	1.4	0.9-2.1	**8**	*12.5*	1.2	0.6-2.4
9	*2.5*	0.7	0.2-2.1	**9**	*2.5*	1.9	0.6-5.7
10	*2.1*	0.9	0.3-2.8	**10**	*2.1*	0.5	0.1-4.3
11	*17.8*	1.1	0.7-1.6	**11**	*17.8*	1.0	0.5-1.9
12	*4.4*	0.9	0.4-1.9	**12**	*4.4*	1.2	0.4-3.4
13	*25.3*	1.1	0.8-1.6	**13**	*25.3*	1.0	0.6-1.8
14	*10.9*	1.0	0.6-1.6	**14**	*10.9*	0.6	0.2-1.6
15	*24.0*	0.9	0.6-1.3	**15**	*24.0*	1.0	0.6-1.9
16	*3.1*	1.3	0.6-2.9	**16**	*3.1*	0.5	0.1-4.3

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 59. Relative frequencies of statistically significant HLA **Class II DRB** allele distributions by allele and **ER status of tumors** in cases vs all controls, white post-menopausal women, Greater Bay Area, 1997-1999

WHITES							
HLA-DRB allele	ER-positive (cases)			HLA-DRB allele	ER-negative (cases)		
	Cases N=114	Controls N=156	p*		Cases N=14	Controls N=156	p*
1				1			
3				3			
4				4			
7				7			
8				8			
9				9			
10				10			
11				11			
12				12			
13				13			
14				14			
15				15			
16				16			

* chi-square or Fisher's exact test

Table 60. Relative frequencies of statistically significant HLA **Class II DRB** allele distributions by allele and **ER status of tumors** in cases vs all controls, black post-menopausal women, Greater Bay Area, 1997-1999

BLACKS							
HLA-DRB allele	ER-positive (cases)			HLA-DRB allele	ER-negative (cases)		
	Cases N=69	Controls N=140	p*		Cases N=37	Controls N=140	p*
1	8.7	10.7	0.65	**1**	**24.3**	**10.7**	**0.03**
3	17.4	25.0	0.22	**3**	**8.1**	**25.0**	**0.03**
4				**4**			
7				**7**			
8				**8**			
9	**0.0**	**7.1**	**0.03**	**9**	2.7	7.1	0.46
10				**10**			
11				**11**			
12				**12**			
13				**13**			
14				**14**			
15				**15**			
16	**4.4**	**0.0**	**0.03**	**16**	0.0	0.0	--

* chi-square or Fisher's exact test

Table 61. Relative frequencies of statistically significant HLA **Class II DRB** allele distributions by allele and **ER status of tumors** in cases vs all controls, Hispanic post-menopausal women, Greater Bay Area, 1997-1999

HISPANICS							
HLA-DRB allele	ER-positive (cases)			HLA-DRB allele	ER-negative (cases)		
	Cases N=94	Controls N=183	p*		Cases N=24	Controls N=183	p*
1				1			
3				3			
4				4			
7				7			
8	**26.6**	**15.3**	**0.02**	8	8.3	15.3	0.54
9	1.1	0.6	1.0	**9**	**12.5**	**0.6**	**0.01**
10				10			
11				11			
12				12			
13				13			
14				14			
15				15			
16				16			

* chi-square or Fisher's exact test

Table 62. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DRB** alleles most strongly with breast cancer risk for **ER positive cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DRB allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
DRB-1		1.0	0.6 – 1.9		0.8	0.3 – 2.3		0.6	0.3 – 1.3
DRB-3		1.0	0.5 – 1.8		0.7	0.3 – 1.5		1.7	0.8 – 3.4
DRB-8		0.7	0.3 – 1.9		1.0	0.4 – 2.6	***15.3***	**2.2**	**1.2 – 4.3**
DRB-9		4.1	0.4 – 41.1		***			3.3	0.2 – 55.4
DRB-16		0.9	0.2 – 3.2		***			0.9	0.2 – 3.0

Table 63. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DRB** alleles most strongly with breast cancer risk for **ER negative cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DRB allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. Prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
DRB-1		0.4	0.04 – 3.0	***10.7***	**2.6**	**1.0 – 6.7**		0.4	0.1 – 1.6
DRB-3		***		***25.0***	**0.3**	**0.1 – 0.97**		2.1	0.7 – 6.6
DRB-8		***			2.1	0.8 – 5.4		0.6	0.1 – 2.7
DRB-9		5.7	0.3–111.6		0.3	0.03 – 2.3	***0.6***	**18.1**	**1.6 – 200.6**
DRB-16		2.1	0.2 – 22.5		0.5	0.1 – 1.7		***	

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 64. Relative frequencies of HLA **Class II DQB-1** allele distributions by allele and breast cancer case-control status by disease stage at diagnosis for cases, and all controls, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-DQB1 allele	Localized stage (cases)			HLA-DQB1 allele	Regional/Remote stage (cases)		
	Cases N=314	Controls N=482	p*		Cases N=108	Controls N=482	p*
2	36.6	33.0	0.29	**2**	33.3	33.0	0.95
3	57.0	57.9	0.81	**3**	50.9	57.9	0.19
4	13.7	13.1	0.80	**4**	10.2	13.1	0.41
5	30.6	30.1	0.88	**5**	35.2	30.1	0.30
6	37.3	38.8	0.66	**6**	43.5	38.8	0.36

* chi-square or Fisher's exact test

Table 65. Adjusted* odds ratios and 95% confidence intervals for associations of HLA **class II DQB1** alleles with breast cancer risk for localized-stage and regional/remote-stage cases vs all controls, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DQB allele	Localized stage (cases)			HLA-DQB allele	Regional/remote (cases)		
	Pop. prev.*	**OR****	**95% CI**		***Pop. prev.****	**OR****	**95% CI**
2	*33.0*	1.1	0.8-1.4	**2**	*33.0*	1.0	0.6-1.6
3	*57.9*	1.0	0.8-1.4	**3**	*57.9*	0.8	0.5-1.2
4	*13.1*	1.2	0.8-1.8	**4**	*13.1*	0.7	0.4-1.5
5	*30.1*	1.0	0.7-1.4	**5**	*30.1*	1.2	0.8-1.9
6	*38.8*	0.9	0.7-1.2	**6**	*38.8*	1.2	0.8-1.8

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 66. Relative frequencies of HLA Class II DQB1 allele distributions by allele and by **disease stage of cases** vs all controls, post-menopausal women by race/ethnicity, Greater Bay Area, 1997-1999

WHITES							
HLA-DQB allele	Localized stage (cases)			HLA-DQB allele	Regional/Remote stage (cases)		
	Cases N=119	Controls N=157	p*		Cases N=33	Controls N=157	p*
2				2			
3				3			
4				4			
5				5			
6				6			

BLACKS							
HLA-DQB allele	Localized stage (cases)			HLA-DQB allele	Regional/Remote stage (cases)		
	Cases N=97	Controls N=140	p*		Cases N=34	Controls N=140	p*
2				2			
3				3			
4				4			
5	**48.5**	**35.7**	**0.05**	5	38.2	35.7	0.78
6				6			

HISPANICS							
HLA-DQB allele	Localized stage (cases)			HLA-DQB allele	Regional/Remote stage (cases)		
	Cases N=98	Controls N=185	p*		Cases N=41	Controls N=185	p*
2	**36.7**	**24.3**	**0.03**	2	24.4	24.3	1.0
3				3			
4	**29.6**	**17.3**	**0.02**	4	12.2	17.3	0.42
5	**15.3**	**26.5**	**0.03**	5	34.2	26.5	0.32
6				6			

* chi-square or Fisher's exact test

Table 67. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DQB** alleles most strongly with breast cancer risk for **localized stage cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DQB allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
DQB-2		1.1	0.6 – 1.7		0.8	0.4 – 1.3	***24.3***	**1.7**	**1.0 – 2.9**
DQB-4		0.9	0.3 – 2.2		0.5	0.2 – 1.3	***17.3***	**2.1**	**1.2 – 3.9**
DQB-5		1.0	0.6 – 1.6	***35.7***	**1.8**	**1.05 – 3.1**	***26.5***	**0.5**	**0.2 – 0.9**

Table 68. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DQB** alleles most strongly with breast cancer risk for **regional/remote stage cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DQB allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. Prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
DQB-2		1.4	0.6 – 3.2		0.8	0.3 – 1.8		1.1	0.5 – 2.5
DQB-4		0.7	0.2 – 3.6		0.8	0.2 – 2.8		0.7	0.2 – 1.9
DQB-5		1.1	0.5 – 2.6		1.0	0.5 – 2.3		1.5	0.7 – 3.2

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer

Table 69. Relative frequencies of HLA **Class II DQB-1** allele distributions by allele and breast cancer case-control status by ER status of tumors for cases, and all controls, all post-menopausal women, Greater Bay Area, 1997-1999

HLA-DQB1 allele	ER-Positive (cases)			HLA-DQB1 allele	ER-Negative (cases)		
	Cases N=282	Controls N=482	p*		Cases N=75	Controls N=482	p*
2	35.8	33.0	0.43	**2**	28.0	33.0	0.39
3	54.6	57.9	0.38	**3**	61.3	57.9	0.57
4	14.2	13.1	0.66	**4**	10.7	13.1	0.56
5	29.4	30.1	0.85	**5**	33.3	30.1	0.57
6	40.4	38.8	0.66	**6**	42.7	38.8	0.52

*chi-square or Fisher's exact test

Table 70. Adjusted* odds ratios and 95% confidence intervals for associations of HLA **class II DQB1** alleles with breast cancer risk for ER-positive and ER-negative cases vs all controls, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DQB allele	ER-Positive (cases)			HLA-DQB allele	ER-Negative (cases)		
	Pop. prev.*	**OR****	**95% CI**		***Pop. prev.****	**OR****	**95% CI**
2	*33.0*	1.1	0.8-1.5	**2**	*33.0*	0.8	0.5-1.5
3	*57.9*	0.9	0.6-1.2	**3**	*57.9*	1.4	0.8-2.3
4	*13.1*	1.2	0.8-1.9	**4**	*13.1*	0.8	0.3-1.8
5	*30.1*	1.0	0.7-1.4	**5**	*30.1*	1.0	0.6-1.7
6	*38.8*	1.0	0.8-1.4	**6**	*38.8*	1.0	0.6-1.8

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 71. Relative frequencies of HLA Class II DQB1 allele distributions by allele and by **ER status of tumors in cases** vs all controls, post-menopausal women by race/ethnicity, Greater Bay Area, 1997-1999

WHITES							
HLA-DQB allele	ER-positive (cases)			HLA-DQB allele	ER-negative (cases)		
	Cases N=117	Controls N=157	p*		Cases N=14	Controls N=157	p*
2				2			
3				3			
4				4			
5				5			
6				6			

BLACKS							
HLA-DQB allele	ER-positive (cases)			HLA-DQB allele	ER-negative (cases)		
	Cases N=69	Controls N=140	p*		Cases N=37	Controls N=140	p*
2	37.7	41.4	0.60	2	**21.6**	**41.4**	**0.03**
3				3			
4				4			
5	42.0	35.7	0.38	5	**54.1**	**35.7**	**0.04**
6				6			

HISPANICS							
HLA-DQB allele	ER-positive (cases)			HLA-DQB allele	ER-negative (cases)		
	Cases N=96	Controls N=185	p*		Cases N=24	Controls N=185	p*
2				2			
3				3			
4	**28.1**	**17.3**	**0.03**	4	16.7	17.3	1.0
5	18.8	26.5	0.15	5	**8.3**	**26.5**	**0.05**
6				6			

* chi-square or Fisher's exact test

Table 72. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DQB** alleles most strongly with breast cancer risk for **ER positive cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DQB allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
DQB-2		1.0	0.6 – 1.7		0.9	0.5 – 1.7		1.5	0.8 – 2.6
DQB-4		1.6	0.9 – 3.0		0.6	0.2 – 1.7	***17.3***	**2.0**	**1.1 – 3.7**
DQB-5		1.1	0.6 – 1.8		1.4	0.7 – 2.6		0.6	0.3 – 1.2

Table 73. Adjusted* odds ratios and 95% confidence intervals for associations of the HLA **class II DQB** alleles most strongly with breast cancer risk for **ER negative cases** vs all controls, by race/ethnicity, post-menopausal women, Greater Bay Area, 1997-1999

HLA-DQB allele	Whites			Blacks			Hispanics		
	Pop. prev.*	**OR****	**95% CI**	***Pop. Prev.****	**OR****	**95% CI**	***Pop. prev****	**OR****	**95% CI**
DQB-2		***		***41.4***	**0.4**	**0.2 – 0.9**		1.4	0.5 – 3.8
DQB-4		***			0.8	0.2 – 2.7		1.0	0.3 – 3.4
DQB-5		***		***35.7***	**2.0**	**1.0 – 4.3**	***26.5***	**0.2**	**0.05 – 0.9**

*Population prevalence=% positive in controls
** adjusted for age at diagnosis, age at menarche, age at first birth, duration of lactation, family history of breast cancer
***unstable model

Table 74. Summary of breast cancer risks associated with **class I A** alleles overall and by disease characteristics, post-menopausal women combined and by racial/ethnic group, Greater Bay Area, 1997-1999

HLA-A Allele	TOTAL		WHITE		BLACK		HISPANIC	
	Overall							
	OR*	95% CI*	OR*	95% CI*	OR*	95% CI*	OR*	95% CI*
A-01	0.9	0.6 – 1.2	1.2	0.7 – 2.0	1.0	0.5 – 2.2	**0.5**	**0.3 – 0.98**
A-23	1.5	0.9 – 2.5	**4.0**	**1.1 –15.0**	1.1	0.6 – 2.1	1.6	0.5 – 4.9
A-32	0.9	0.5 – 1.6	0.7	0.3 – 1.6	**10.0**	**1.2 – 82.5**	0.3	0.1 – 1.1
A-33	**1.8**	**1.0 – 3.2**	1.5	0.4 – 5.5	**2.4**	**1.0 – 5.6**	1.7	0.6 – 4.9
	By stage							
HLA-A Allele	**local**	**remote**	**local**	**remote**	**Local**	**remote**	**local**	**remote**
	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI
A-01	**0.7 0.5–0.99**	1.3 0.8–2.2	1.0 0.6–1.8	1.8 0.8– 4.0	0.7 0.3 – 1.7	1.7 0.6 – 5.2	**0.3 0.1 – 0.7**	1.1 0.5– 2.6
A-11	0.9 0.5–1.4	**0.3 0.1–1.0**						
A-23	**1.7 1.1–2.8**	0.7 0.3–1.8	**4.2 1.1–16.5**	0.9 0.3– 2.9	1.4 0.7 – 2.7	0.6 0.1 – 2.0	2.3 0.7 – 7.2	***
A-30	0.8 0.5–1.2	**1.9 1.0–3.4**						
A-32	1.0 0.6–1.8	0.8 0.3–2.4	0.6 0.2–1.5	1.1 0.3– 4.2	**12.1 1.4–103**	6.4 0.3–127	0.4 0.1 – 1.6	***
A-33	**2.3 1.3–4.1**	1.3 0.5–3.3	1.7 0.4–6.8	1.0 0.1–10.0	**3.0 1.3 – 7.3**	1.0 0.2 – 5.1	1.6 0.4 – 5.4	1.9 0.4– 7.9
	By ER status							
HLA-A Allele	**ER-pos**	**ER-neg**	**ER-pos**	**ER-neg**	**ER-pos**	**ER-neg**	**ER-pos**	**ER-neg**
	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI
A-01	0.9 0.6 – 1.3	0.5 0.2–1.1						
A-11	**0.4 0.2 – 0.8**	1.5 0.6–3.6	**0.4 0.2–0.9**	***	0.7 0.1–7.0	3.0 0.5–18.8	0.4 0.1 – 1.4	1.0 0.2 – 5.1
A-23	1.6 0.9 – 2.8	1.1 0.4–2.6	**4.3 1.1–16.9**	***	0.9 0.4–2.0	1.3 0.5–3.4	2.2 0.7 – 7.1	1.0 0.1 – 9.3
A-24	0.8 0.5 – 1.2	0.7 0.3–1.5	**0.4 0.2–0.9**	***	0.8 0.2–2.6	0.4 0.04-3.0	1.1 0.6 – 2.0	0.8 0.3 – 2.3
A-32	1.1 0.6 – 2.1	0.6 0.1–2.8	0.9 0.3–2.1	***	**12.6 1.4-15.2**	9.3 0.7-118	0.4 0.1 – 1.6	***
A-33	1.8 0.9 – 3.5	**2.8 1.2–6.6**	2.1 0.6–7.8	***	1.4 0.5–4.2	**5.9 2.0–17.2**	2.4 0.8 – 7.4	1.1 0.1 – 9.4

*OR: odds ratio

*CI: Confidence Interval

Table 75. Summary of breast cancer risks associated with **class I B** alleles overall and by disease characteristics, post-menopausal women combined and by racial/ethnic group, Greater Bay Area, 1997-1999

HLA-B Allele	TOTAL		WHITE		BLACK		HISPANIC	
	Overall							
	OR*	95% CI*	OR*	95% CI*	OR*	95% CI*	OR*	95% CI*
B-07	1.1	0.8 – 1.6	1.3	0.8 – 2.3	1.8	0.9 – 3.5	**0.5**	**0.2 – 0.96**
B-13	**0.5**	**0.2 – 0.99**	0.4	0.1 – 1.2	0.4	0.1 – 2.4	0.6	0.1 – 2.5
B-39	**0.6**	**0.3 – 0.99**	0.4	0.1 – 1.6	1.2	0.3 – 5.9	0.5	0.3 – 1.1
B-40	1.3	0.9 – 2.0	1.2	0.6 – 2.3	1.0	0.3 – 3.4	**1.8**	**1.0 – 3.1**
B-45	0.6	0.3 – 1.2	1.0	0.1 – 7.4	0.7	0.3 – 1.6	**0.1**	**0.01 – 1.0**
	By stage							
HLA-B Allele	**local**		**remote**		**local**		**remote**	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
B-13	0.4	0.2-1.0	0.6	0.2-2.1				
B-15	**1.5**	**1.0-2.2**	1.0	0.5-1.8	1.7	0.8 – 3.4	0.5	0.1–2.6
B-35	0.8	0.6-1.2	1.4	0.9-2.4	0.8	0.4 – 1.5	0.9	0.3–2.7
B-39	0.6	0.3-1.2	0.5	0.2-1.2				
B-40	1.3	0.9-2.0	1.4	0.8-2.6	1.1	0.5 – 2.2	1.4	0.5–4.3
B-58	1.4	0.8-2.6	0.9	0.3-2.5	***		5.2	0.6–42.7
HLA-B Allele	**Local**		**remote**		**local**		**remote**	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
B-13								
B-15	1.2	0.6 – 2.2	0.5	0.2 – 1.6	1.7	0.8–3.8	2.2	0.8 – 5.8
B-35	0.8	0.3 – 1.9	0.7	0.2 – 2.7	1.3	0.7–2.3	**2.2**	**1.1 – 4.6**
B-39								
B-40	0.6	0.1 – 2.9	2.2	0.5 – 10.0	**1.9**	**1.03–3.6**	1.5	0.6 – 3.8
B-58	1.5	0.7 – 3.2	0.6	0.2 – 2.3	2.8	0.6–13.4	1.5	0.1 – 16.0
	By ER status							
HLA-B Allele	**ER-pos**		**ER-neg**		**ER-pos**		**ER-neg**	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
B-07	1.2	0.8-1.8	1.2	0.6-2.5	1.2	0.6–2.1	***	
B-41	1.6	0.5-5.5	**4.5**	**1.2-17.8**	3.9	0.4–38.4	***	
B-52	0.6	0.2-1.6	1.9	0.6-5.5	0.8	0.2–3.6	***	
HLA-B Allele	**ER-pos**		**ER-neg**		**ER-pos**		**ER-neg**	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
B-07	**2.3**	**1.1 – 5.0**	1.1	0.4–3.5	0.5	0.2–1.2	0.5	0.1 – 2.1
B-41	***		3.0	0.4–21.2	2.4	0.3–18.3	**13.5**	**1.6 – 111.5**
B-52	***		0.6	0.1–5.6	0.9	0.2–3.5	**5.6**	**1.4 – 22.9**

*OR: odds ratio

*CI: Confidence Interval

Table 76. Summary of breast cancer risks associated with **class II DRB** alleles overall and by disease characteristics, post-menopausal women combined and by racial/ethnic group, Greater Bay Area, 1997-1999

HLA-DRB Allele	TOTAL		WHITE		BLACK		HISPANIC	
	Overall							
	OR*	95% CI*	OR*	95% CI*	OR*	95% CI*	OR*	95% CI*
DRB9	1.0	0.4 – 2.3	4.3	0.5 –38.5	**0.2**	**0.04 –0.8**	5.7	0.6 – 53.5
	By stage							
HLA-DRB Allele	local	remote	local	remote	Local	remote	local	remote
	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI
DRB3	1.0 (0.7-1.4)	1.2 (0.7-2.0)	1.1 (0.6 – 2.0)	1.4 (0.5–3.6)	**0.5 (0.2 – 1.0)**	1.2 (0.5 – 2.9)	1.7 (0.8 – 3.3)	1.4 (0.5 – 3.9)
DRB8	1.3 (0.9-2.0)	1.0 (0.5-1.9)	0.8 (0.3 – 2.0)	0.3 (0.04–2.5)	1.2 (0.5 – 2.6)	2.2 (0.8 – 5.9)	**2.3 (1.2 – 4.4)**	0.6 (0.2 – 1.9)
DRB16	1.0 (0.4-2.2)	1.5 (0.5-4.5)	0.6 (0.1 – 2.6)	2.7 (0.6–12.3)	***	0.4 (0.1 – 1.8)	0.4 (0.1 – 2.0)	1.0 (0.2 – 5.0)
	By ER status							
HLA-DRB Allele	ER-pos	ER-neg	ER-pos	ER-neg	ER-pos	ER-neg	ER-pos	ER-neg
	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI
DRB1	0.9 (0.6-1.3)	1.0 (0.5-2.1)	1.0 (0.6–1.9)	0.4 (0.04–3.0)	0.8 (0.3 – 2.3)	**2.6 (1.0–6.7)**	0.6 (0.3–1.3)	0.4 (0.1–1.6)
DRB3	1.0 (0.7-1.5)	0.9 (0.5-1.8)	1.0 (0.5–1.8)	***	0.7 (0.3 – 1.5)	**0.3 (0.1–0.97)**	1.7 (0.8–3.4)	2.1 (0.7–6.6)
DRB8	1.4 (0.9-2.1)	1.2 (0.6-2.4)	0.7 (0.3–1.9)	***	1.0 (0.4 – 2.6)	2.1 (0.8–5.4)	**2.2 (1.2–4.3)**	0.6 (0.1–2.7)
DRB9	0.7 (0.2-2.1)	1.9 (0.6-5.7)	4.1 (0.4–41.1)	5.7 (0.3–112)	***	0.3 (0.03–2.3)	3.3 (0.2–55.4)	**18.1 (1.6–201)**
DRB16	1.3 (0.6-2.9)	0.5 (0.1-4.3)	0.9 (0.2–3.2)	2.1 (0.2–22.5)	***	0.5 (0.1–1.7)	0.9 (0.2–3.0)	***

*OR: odds ratio

*CI: Confidence Interval

Table 77. Summary of breast cancer risks associated with **class II DQB** alleles overall and by disease characteristics, post-menopausal women combined and by racial/ethnic group, Greater Bay Area, 1997-1999

HLA-DQB Allele	TOTAL		WHITE		BLACK		HISPANIC	
	Overall							
	OR*	95% CI*	OR*	95% CI*	OR*	95% CI*	OR*	95% CI*
DQB5	1.1	0.8 – 1.4	1.0	0.6 – 1.7	**1.6**	**0.97 –2.6**	0.7	0.4 – 1.2
	By stage							
HLA-DQB Allele	Local	remote	local	remote	Local	remote	local	remote
	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI
DQB2	1.1 (0.8-1.4)	1.0 (0.6-1.6)	1.1 (0.6 – 1.7)	1.4 (0.6–3.2)	0.8 (0.4 – 1.3)	0.8 (0.3 – 1.8)	**1.7 (1.0 – 2.9)**	1.1 (0.5 – 2.5)
DQB4	1.2 (0.8-1.8)	0.7 (0.4-1.5)	0.9 (0.3 – 2.2)	0.7 (0.2–3.6)	0.5 (0.2 – 1.3)	0.8 (0.2 – 2.8)	**2.1 (1.2 – 3.9)**	0.7 (0.2 – 1.9)
DQB5	1.0 (0.7-1.4)	1.2 (0.8-1.9)	1.0 (0.6 – 1.6)	1.1 (0.5–2.6)	**1.8 (1.05 – 3.1)**	1.0 (0.5 – 2.3)	**0.5 (0.2 – 0.9)**	1.5 (0.7 – 3.2)
	By ER status							
HLA-DQB Allele	ER-pos	ER-neg	ER-pos	ER-neg	ER-pos	ER-neg	ER-pos	ER-neg
	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI	OR / 95% CI
DQB2	1.1 (0.8-1.5)	0.8 (0.5-1.5)	1.0 (0.6 – 1.7)	***	0.9 (0.5 – 1.7)	**0.4 (0.2–0.9)**	1.5 (0.8 – 2.6)	1.4 (0.5–3.8)
DQB4	1.2 (0.8-1.9)	0.8 (0.3-1.8)	1.6 (0.9 – 3.0)	***	0.6 (0.2 – 1.7)	0.8 (0.2–2.7)	**2.0 (1.1 – 3.7)**	1.0 (0.3–3.4)
DQB5	1.0 (0.7-1.4)	1.0 (0.6-1.7)	1.1 (0.6 – 1.8)	***	1.4 (0.7 – 2.6)	**2.0 (1.0–4.3)**	0.6 (0.3 – 1.2)	**0.2 (0.05–0.9)**

*OR: odds ratio

*CI: Confidence Interval

Table 78. Case counts and average annual age-specific incidence rates per 100,000 of female invasive breast cancer, 1997-1999, Greater Bay Area residents, by race/ethnicity

Age at Diagnosis	All Women		White		Black		Hispanic	
	Count	**Rate***	**Count**	**Rate***	**Count**	**Rate***	**Count**	**Rate***
50-54	1,626	273.4	1,157	314.0	94	225.6	156	217.0
55-59	1,559	359.6	1,114	414.9	87	276.3	143	272.1
60-64	1,391	399.1	995	485.6	84	333.7	122	282.4
65-69	1,407	444.9	1,053	560.5	76	348.4	110	297.7
70-74	1,406	468.7	1,089	565.1	57	299.9	110	368.8
75-79	1,359	525.1	1,086	598.8	86	513.0	82	396.5

* per 100,000

Table 79. Results of published studies on breast cancer risk and HLA class I and II alleles examined by DNA genotyping

Authors	Ethnicity/ nationality	Age	Study design	Sample size		Alleles analyzed	Alleles associated	Case and control prevalences, p-value	Measure of association
				Cases	Controls				
Chaudhuri et al.[27]	White American	<40	Hospital- based	176	215	DQB1, DPB1, DRB	DQB1*03032	0.0% vs 7.0%, p=0.003*	RR=0.04, p=0.0002
							DRB1*11	3.5% vs 16.3%, p=0.002*	RR=0.18, p=0.003
							DRB3*0201	55% vs 41%, p=0.02*	
Ghaderi et al.[32]	Iranian	unk	Hospital cases, community controls	36	36	DRB1	DRB1*12	50% vs 3%, p=0.03	
Baccar Harrath et al.[34]	Tunisian	27-67	Hospital cases, community controls	70	70	DRB1, DQB1	DR*07-DQ*02	6.4% vs 15.7%, p=0.01	OR=0.4, 95% CI 0.2 – 0.9
Laumbacher and Wank[33]	German	unk	unspecified	51	407	DQB1	DQB1*0201	25.5% vs 8.1%, p=0.006	
Lavado et al.[35]	Spanish	unk	Hospital- based	132	382	A, B, Cw, DR, DQ	B*07	28% vs 15%, p=0.03*	RR=2.1, 95% CI 1.3 – 3.4
Gopalkrishnan et al.[36]	Indian	Pre-meno	Hospital cases, community controls	81	160	Class I	A*11	18.0% vs 11.3%, p<0.05*	
							B*40	16.0% vs 9.0%	OR=2.2, 95% CI 1.2 – 4.3, p=0.38*

* corrected for multiple comparisons